بسم الله الرحمن الرحيم

EMBRYOLOGY

Embryology | Lecture 2

Malformation of The Respiratoy Tract

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﴿ وَلَقَدْ نَعْلَمُ أَنَّكَ يَضِيقُ صَدْرُكَ بِمَا يَقُولُونَ ﴿٩٧﴾ فَسَبِّحْ بِحَمْدِ رَبِّكَ وَكُن مِّنَ السَّاجِدِينَ ﴾

سبحان الله وبحمده، سبحان الله العظيم

وَلِلَّهِ الْأَسْمَاءُ الْحُسْنَى فَادْعُوهُ بِهَا

المعنى: الذي خضعت له الرقاب، وذلت له الجبابرة، وعنت له الوجوه، وقهر كل شيء، ودانت له الخلائق وتواضعت لعظمته وجلاله وكبريائه.

الورود: ورد اسم القاهر مرتين، أما اسم القهار فورد (٦) مرات.

الشاهد: ﴿ وَهُوَ ٱلْوَٰحِدُ ٱلْقَهَّٰرُ ﴾ [الرعد:١٦]، ﴿وَهُوَ ٱلْقَاهِرُ فَوْقَ عِبَادِهِۦ﴾ [الأنعام:١٨].

٦٣

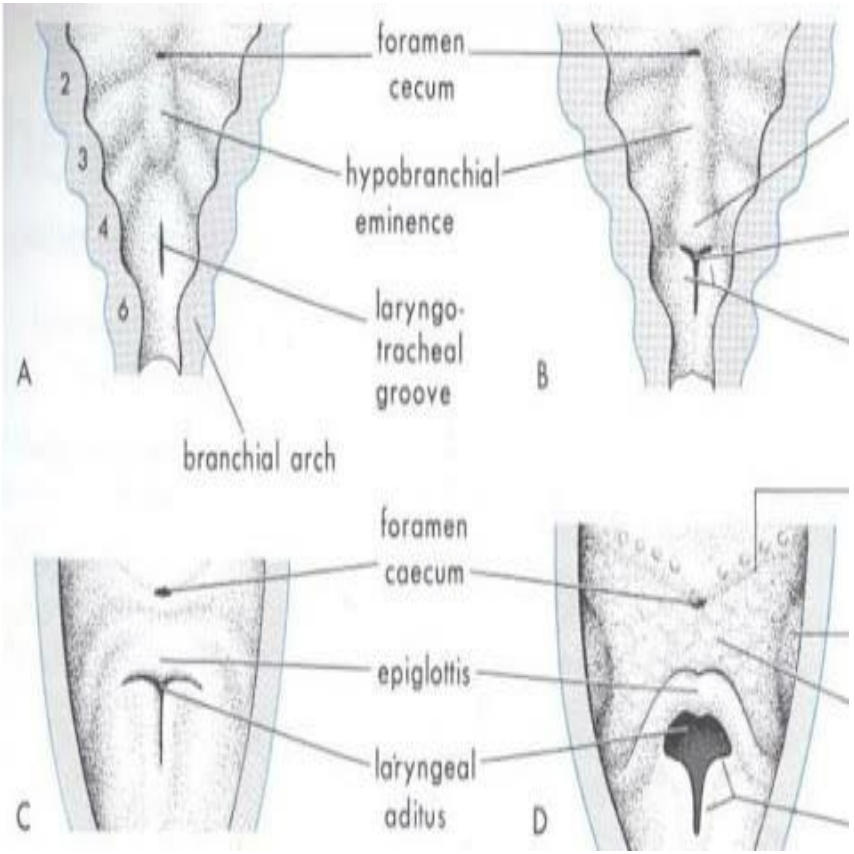
اضغط هنا لشرحٍ أكثر تفصيلًا

Lungs and Bronchial tree development

Reminder: Tracheoesophageal Separation

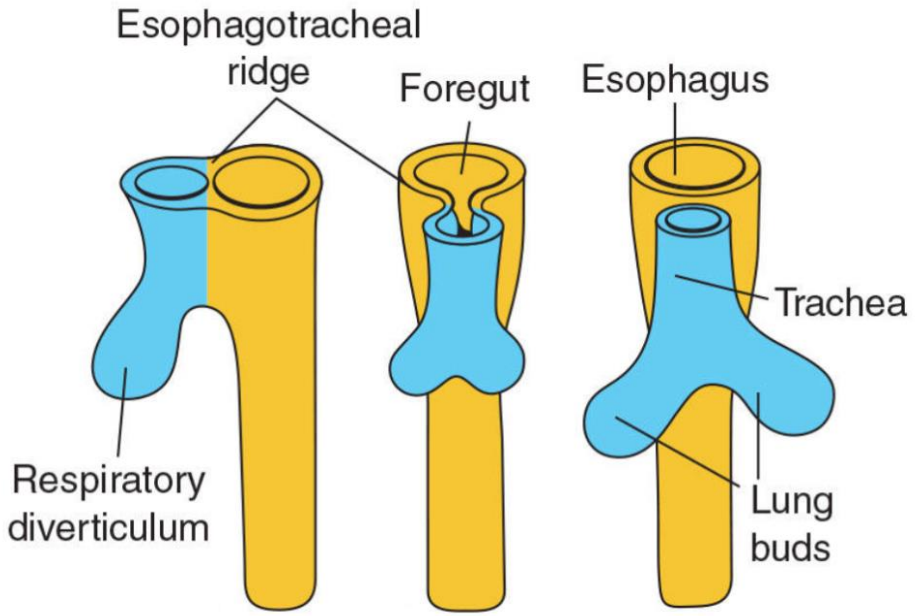
- The respiratory diverticulum arises from the anterior wall of the foregut. A separation process then occurs to divide the respiratory and digestive systems. This separation begins with a longitudinal cleft (fold) that later develops into the tracheoesophageal septum, which completely separates the trachea from the esophagus.

- The only remaining connection is the laryngeal inlet, which connects the pharynx to the larynx, and changes from a slit-like opening to a T-shaped, and finally to a permanent heart-shaped opening.



Trachea, Bronchi, and Lungs

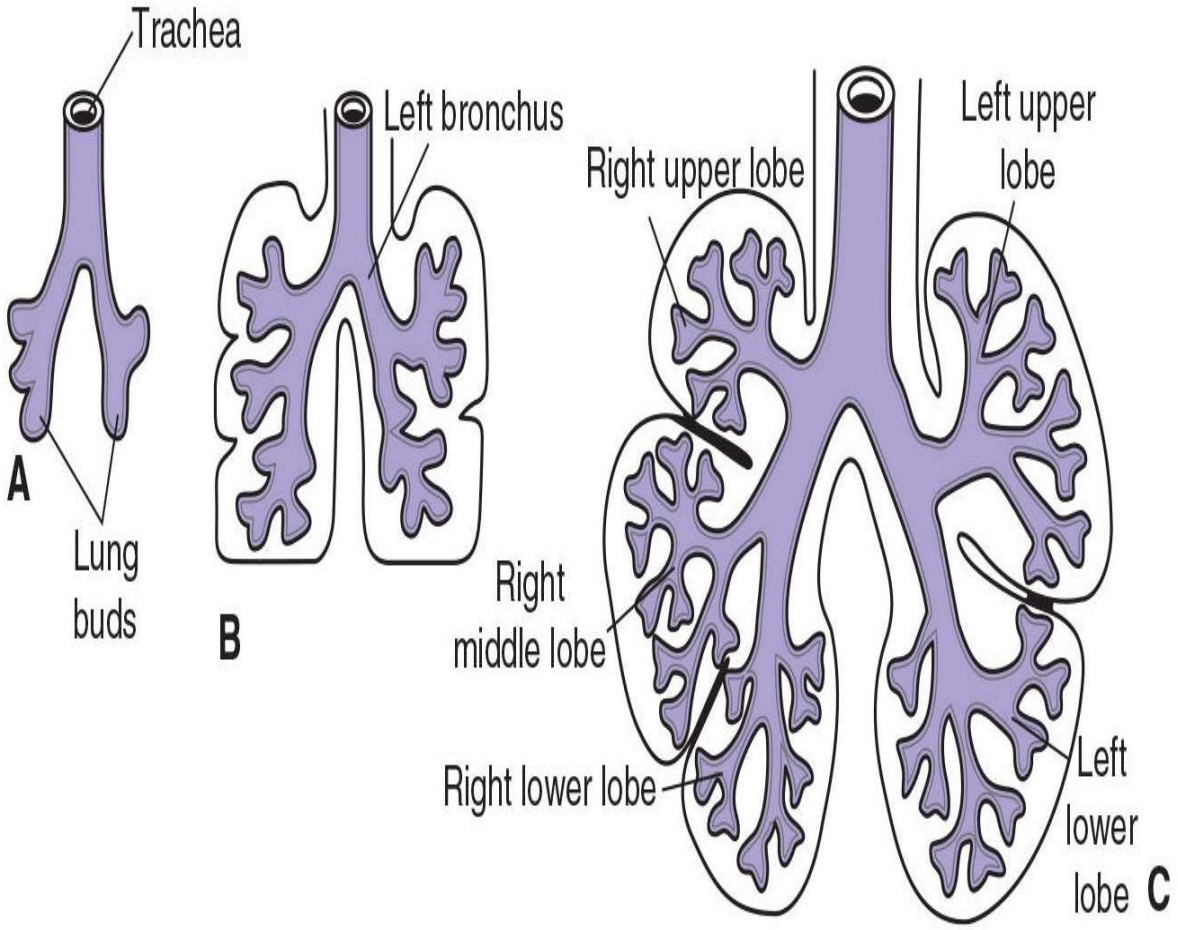
- The trachea develops from the bronchial buds, which were initially called lung buds, arising from the endoderm of the anterior foregut. First, proliferation of endodermal cells forms the epithelial lining of the trachea, while the cartilage, smooth muscle, and connective tissues are derived from the surrounding splanchnic mesoderm. As development continues, the trachea elongates caudally, and at the level of T4 it divides into the primary (main) bronchi.



Dr.'s figure:

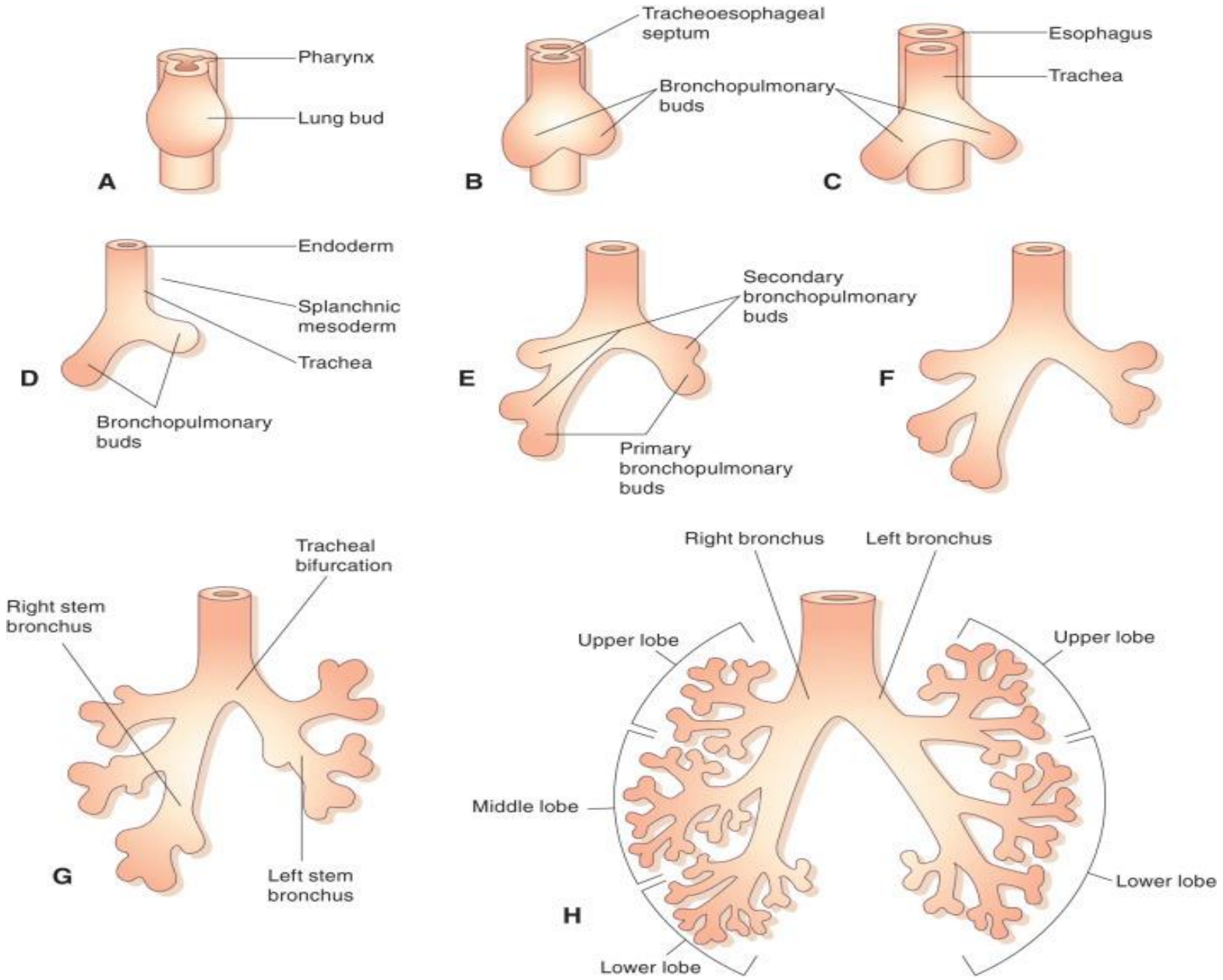
Trachea, Bronchi, and Lungs

- The primary bronchi then divide into **secondary bronchi**, three on the right and two on the left, which are called **lobar bronchi** according to the lung lobes.
- The secondary bronchi further divide into **tertiary** (segmental) bronchi, each of which supplies a bronchopulmonary segment. There are 10 bronchopulmonary segments in the right lung and usually 8–10 in the left lung.



Dr.'s figure:

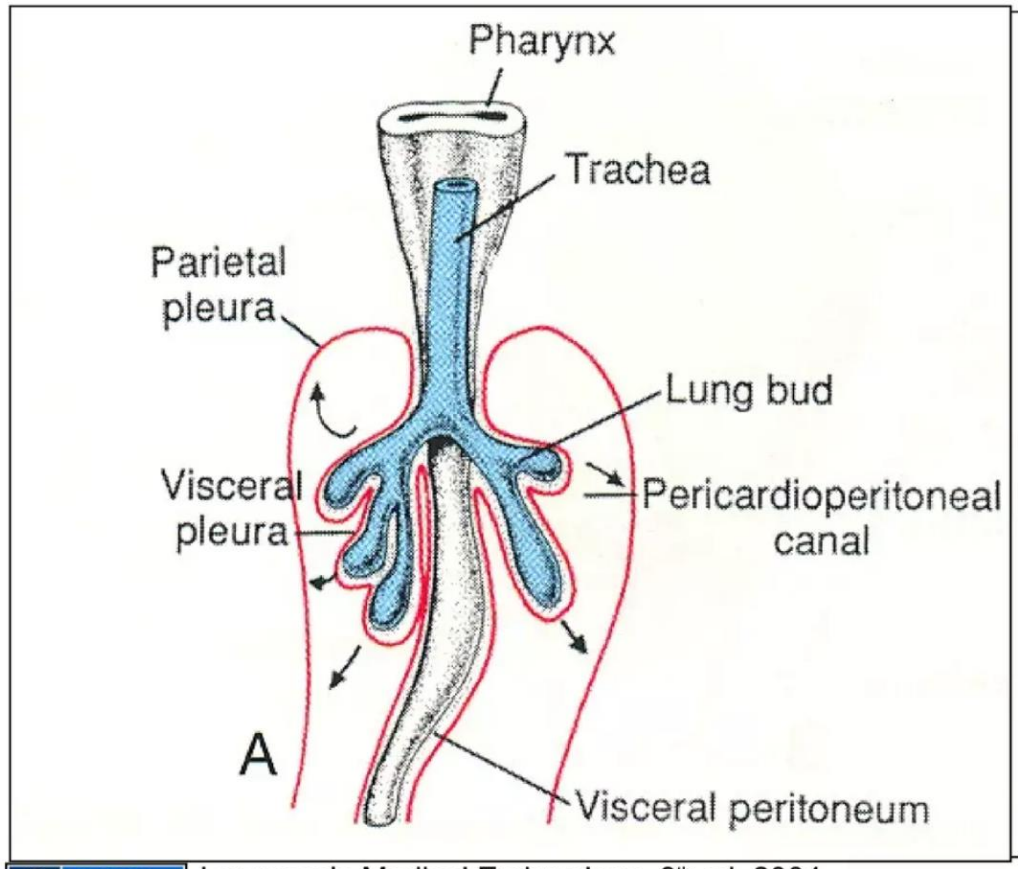
Extra Image: Bronchial Tree Development



Trachea, Bronchi, and Lungs

- After the tertiary bronchi, the airways divide into bronchioles, which are of two types: conducting and respiratory.
- Conducting bronchioles further divide in a dichotomous pattern, forming tree-like branches.
- This branching occurs in an open space called the **pericardioperitoneal canal**.

- With growth in caudal and lateral directions, the lung buds expand into the body cavity.
- The spaces for the lungs and pericardioperitoneal canals become narrow.
- These canals lie on each side of the foregut.

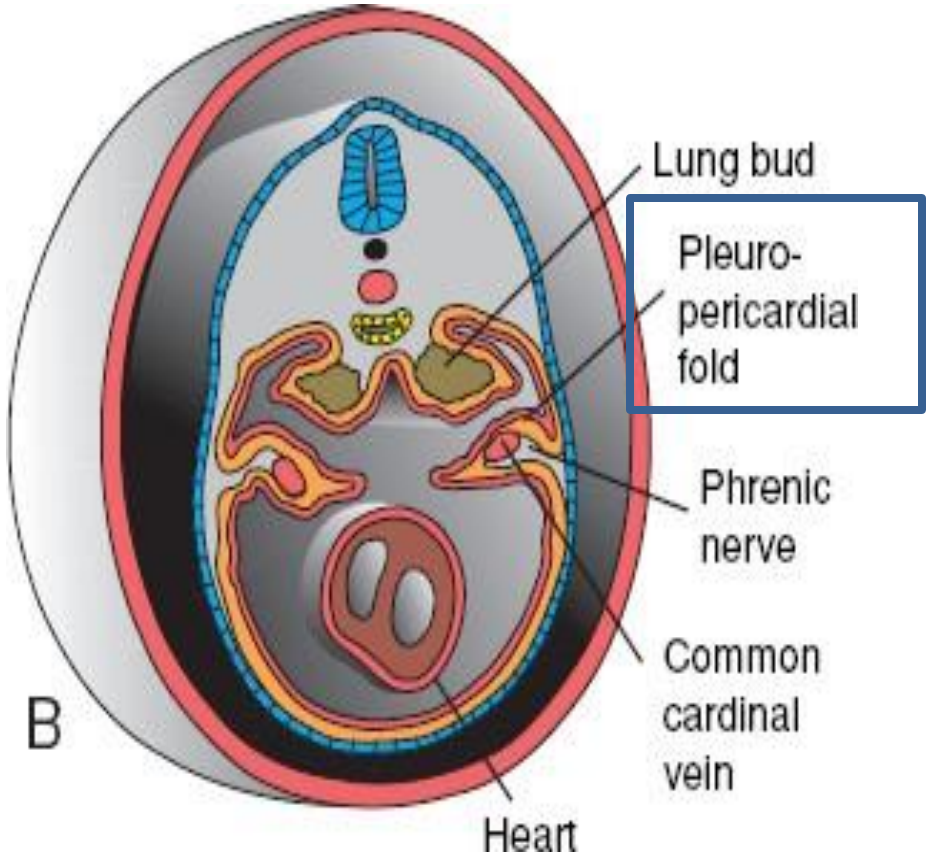


 Langman's Medical Embryology, 9th ed. 2004.

Dr.'s figure:

Trachea, Bronchi, and Lungs

- The intraembryonic coelom is subdivided into three compartments: the pericardial cavity, two pleural cavities, and the peritoneal cavity.
- Ultimately, the pleuropericardial folds separate the pleural cavities from the pericardial cavity, and the pleuroperitoneal folds separate the pleural cavities from the peritoneal cavity.
- The pericardioperitoneal canals persist as the primitive pleural cavities.

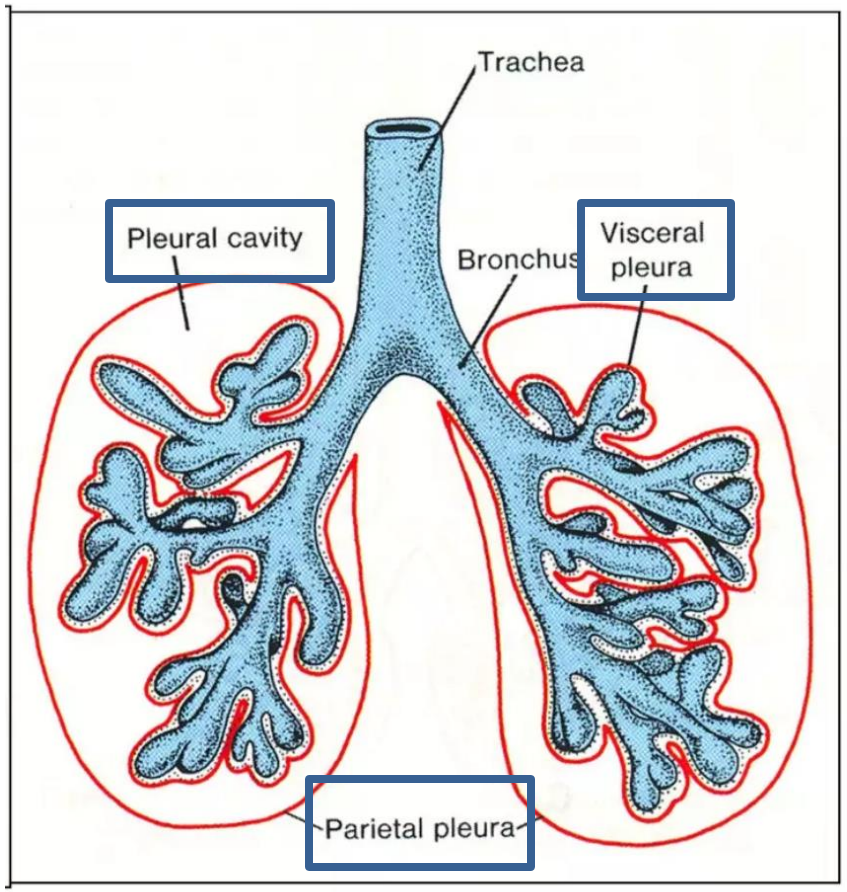


Dr.'s figure:

Trachea, Bronchi, and Lungs

The pleural cavity consists of:

- The splanchnic 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



Dr.'s figure:

Trachea, Bronchi, and Lungs

- During further development, secondary bronchi divide repeatedly in a dichotomous fashion, forming 10 **tertiary (segmental)** bronchi in the right lung and 8 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.

- Before the bronchial tree reaches its final shape, however, **an additional 6 divisions form during postnatal life. Resulting in a total of 23 generations of branching.**

- Signals for branching, which emit from the mesoderm, involve members of the fibroblast growth factor (FGF) family, which stimulate cell division and proliferation.

Maturation of the Lungs

Lung maturation refers to the development and functional differentiation of distal lung structures beyond the bronchioles. This process involves the formation of respiratory bronchioles, followed by alveolar ducts, alveolar sacs, and eventually alveoli. The alveolar–capillary (respiratory) membrane then develops within the alveoli, making them the primary sites of gas exchange.

Lung maturation consists of 4 stages:

TABLE 12.1 Maturation of the Lungs

Pseudoglandular period	5–16 weeks (4 months)	Branching has continued to form terminal bronchioles. No respiratory bronchioles or alveoli are present.
Canalicular period	16–26 weeks (6 months)	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 (7-9)	Terminal sacs (primitive alveoli) form, and capillaries establish close contact.
Alveolar period	8 months to childhood (8 months-10 years)	Mature alveoli have well-developed epithelial endothelial (capillary) contacts.

The respiratory membrane have not developed yet.

The respiratory membrane have not developed yet.

At this stage, the respiratory membrane is developing.

Clinical Implications of Lung Maturation Stages

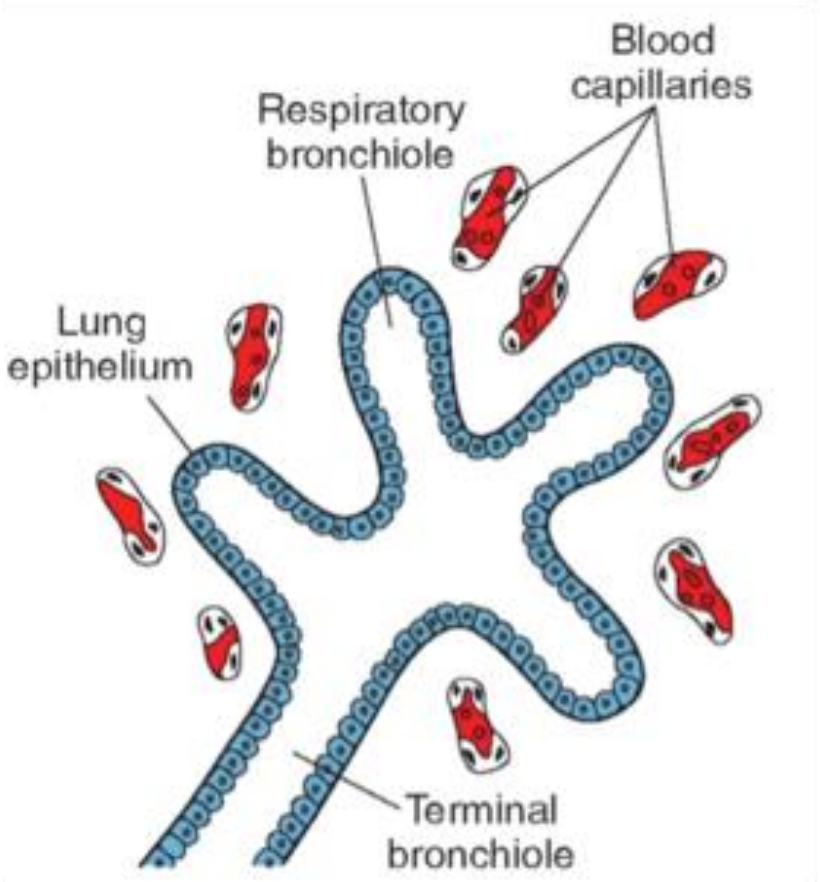
- The viability of a neonate is primarily governed by the progressive development of the respiratory membrane.
- During the **pseudoglandular stage,** survival is impossible due to the absence of gas-exchange membranes.
- In the **late canalicular stage**, survival becomes possible, but it requires intensive care, including exogenous surfactant administration and mechanical ventilation.
- By the terminal saccular stage, the expansion of terminal sacs significantly improves prognosis.
- In the **alveolar stage**, the lungs undergo extensive alveolarization until approximately 10 years of age. Notably, only about one-sixth of the adult number of alveoli are present at birth, while the remaining five-sixths develop postnatally. During this stage, alveoli increase in number and maturity, leading to more efficient and well-defined respiratory membranes for gas exchange.

Maturation of the Lungs

- Up to the seventh prenatal month, the bronchioles divide continuously into more and smaller canals (canalicular phase)

•In this stage, most cells are cuboidal, and the capillaries are distant from the air spaces.

- Respiration becomes possible when some of the cells of the cuboidal **respiratory bronchioles** change into thin, flat cells.

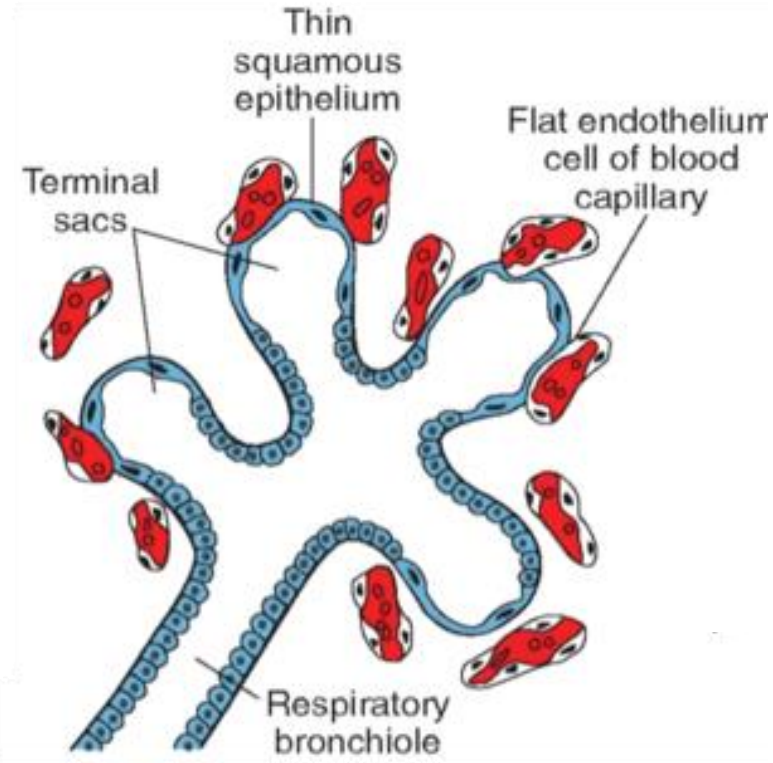


Canalicular Period

Dr.'s figure:

Maturation of the Lungs

- Some of the cuboidal cells thin out into simple squamous cells.
- 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.**

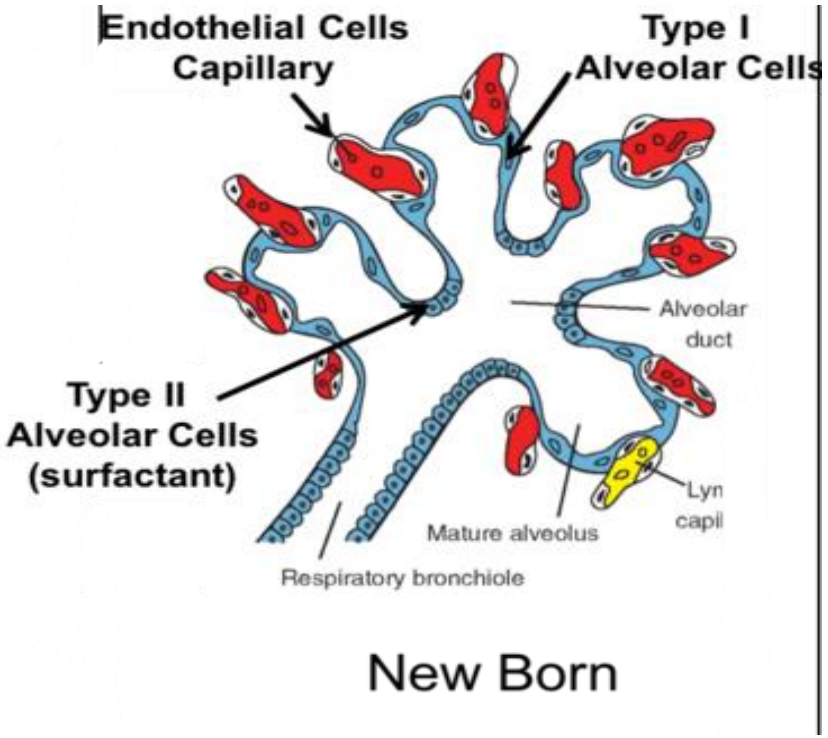


Terminal Sac Period

Dr.'s figure:

Maturation of the Lungs

- During the last 2 months of prenatal life and for several years thereafter, the number of terminal sacs increases steadily.
- In addition, cells lining the sacs, known as **type I alveolar epithelial cells,** become thinner, so that surrounding capillaries protrude into the alveolar sacs
- This intimate contact between epithelial and endothelial cells makes up the **blood-air barrier.**
- During the last two months, Type II cells mature and surfactant production increases significantly.
- **Mature alveoli** are not present before birth.



New Born

Dr.'s figure:

Maturation of the Lungs

- 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, which reduces surface tension of alveoli, allowing for alveolar inflation during expiration.**

- Before birth the lungs are full of fluid that contains a high chloride concentration, little protein, some mucus from the bronchial glands, and surfactant from the alveolar epithelial cells (type II)

- The amount of surfactant in the fluid increases, particularly during the last 2 weeks before birth.

Maturation of the Lungs

- Fetal **breathing movements** begin before birth and cause aspiration of amniotic fluid
- 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 during expiration (atelectasis).**

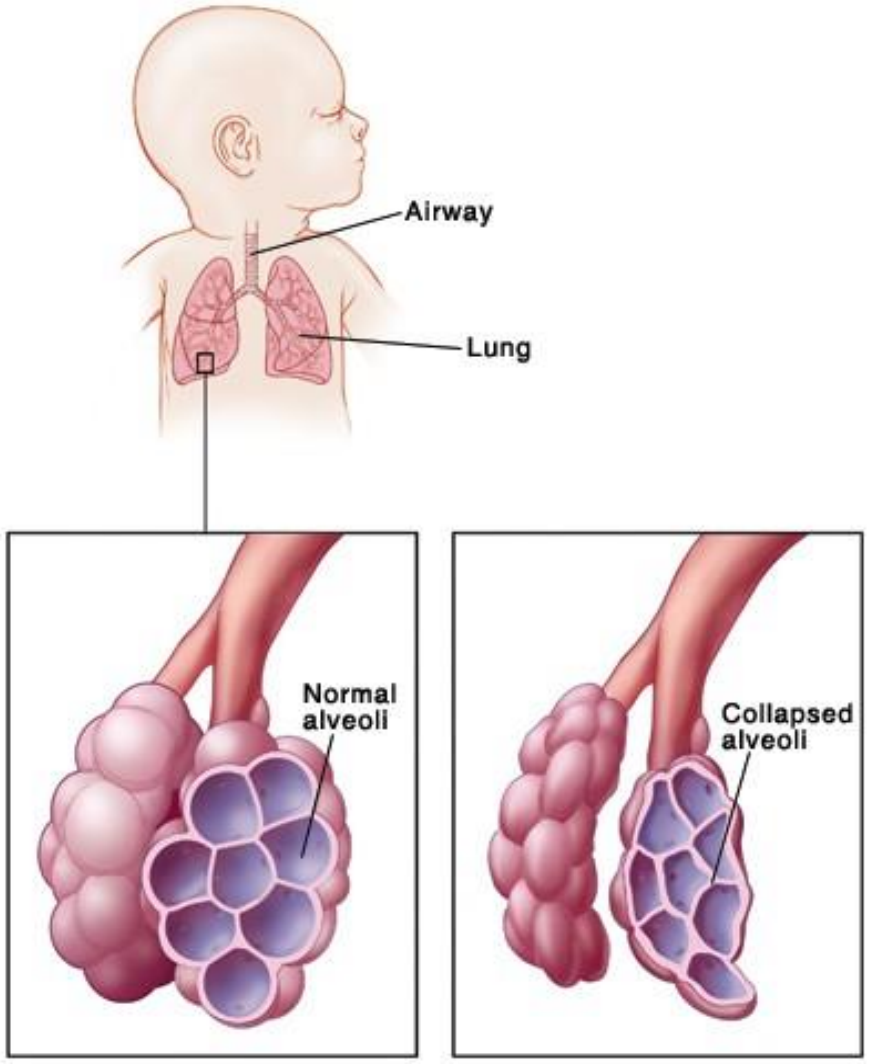
Maturation of the Lungs

- Respiratory movements after birth bring air into the lungs, which expand and fill the pleural cavity.
- Although the alveoli increase slightly in size, postnatal lung growth is due primarily to an increase in the number of respiratory bronchioles and alveoli.
- If surfactant levels are insufficient, medical intervention is necessary to prevent respiratory distress. There is synthetic (exogenous) surfactant that can be directly administered to the neonate's lungs via endotracheal tube.
- Alternatively, surfactant production can be stimulated prenatally using medications such as **Betamethasone** (a corticosteroid) given to the mother.
- Additionally, **Thyroxine** (thyroid hormone) also plays a crucial role in stimulating the maturation of Type II cells and increasing surfactant secretion.

Anomalies of the lung

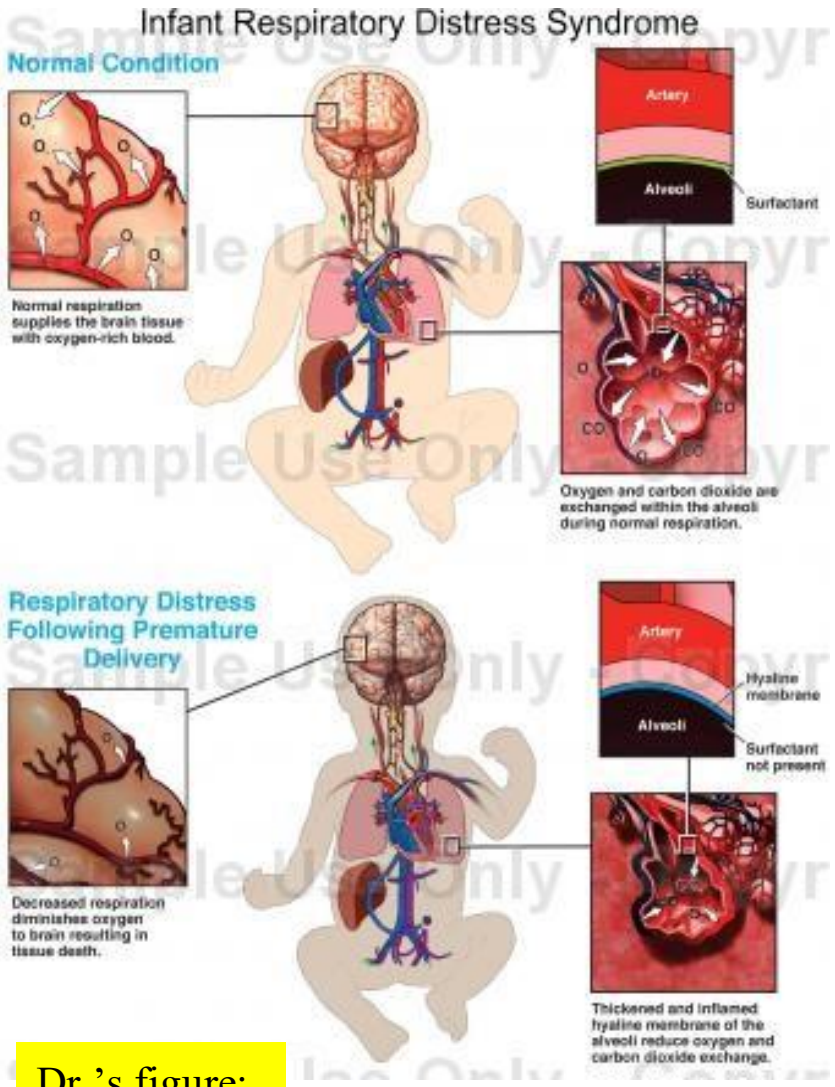
Clinical notes (RDS)

- 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.



Clinical notes (RDS)

- 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) to stimulate surfactant production have reduced the mortality associated with RDS.
- **It Also allowed survival of some babies as young as 5.5 months of gestation.**
- Thyroxine is the most important stimulator for surfactants production.



Dr.'s figure:

Clinical notes (Other Anomalies)

- Although many abnormalities of the lung and bronchial tree have been found (e.g., blind-ending trachea with **absence of lungs and agenesis of one lung**) most of these gross abnormalities are rare.

- **Abnormal divisions of the bronchial tree are more common; some result in supernumerary lobules.**

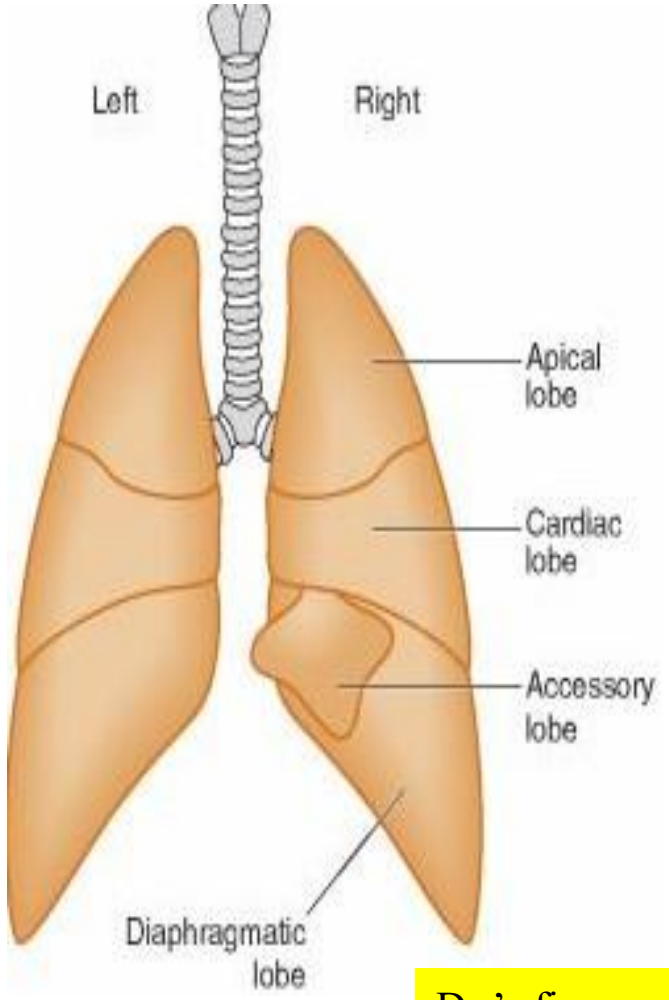
- These variations of the bronchial tree have little functional significance, but they may cause unexpected difficulties during bronchoscopies.

Clinical notes (Other Anomalies)

- **ectopic lung lobes** arising from the trachea or esophagus.

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

- **No serious outcomes.**

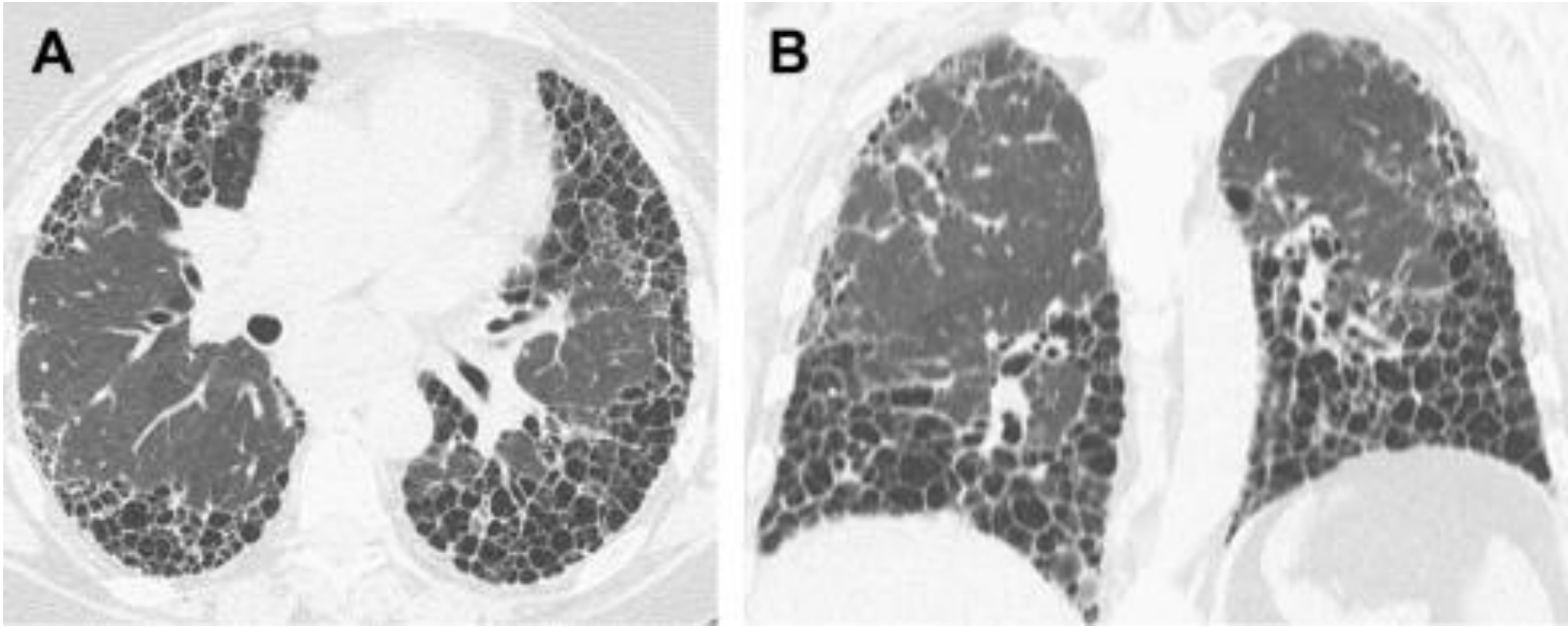


Dr.'s figure:

Clinical notes (Other Anomalies)

- Most important clinically are **congenital cysts of the lung.**
- which are formed by dilation of terminal or larger bronchi.
- **These cysts may be small and multiple, giving the lung a honeycomb appearance on radiograph.** (Refer to next page).
- Or they may be restricted to one or more larger ones.
- Cystic structures of the lung usually drain poorly and **frequently cause chronic infections, and insufficient gas exchange.**
- **Treated by surgical excision.**

Dr.'s figure:


A
B

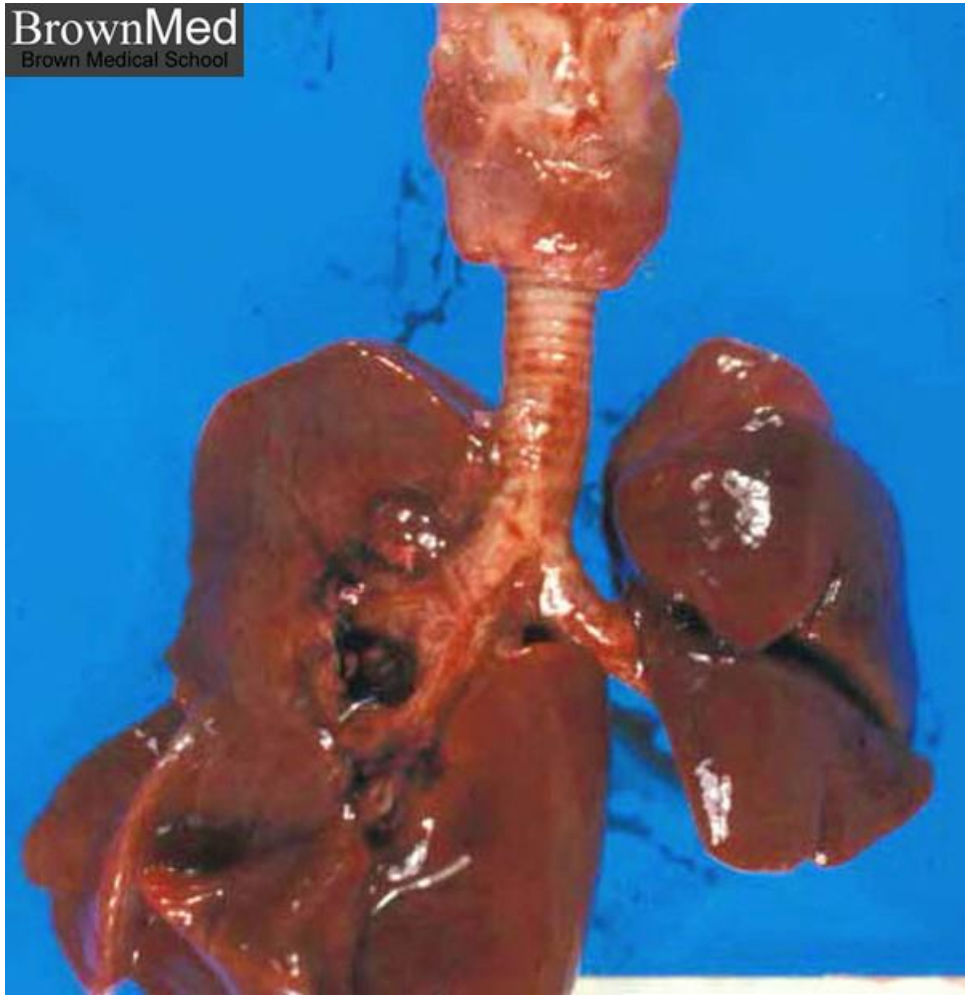
Lung Hypoplasia

- Reduced lung size, due to one of the following causes:

1. In infants with congenital diaphragmatic hernia (CDH) the lung is unable to develop normally. This condition is more common on the left side. 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.



Oligohydroamnios and lungs

2. When oligohydroamnios (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 **float in water.**

- The lungs of the stillborn infants are firm and sink in water because they contain fluids not air.

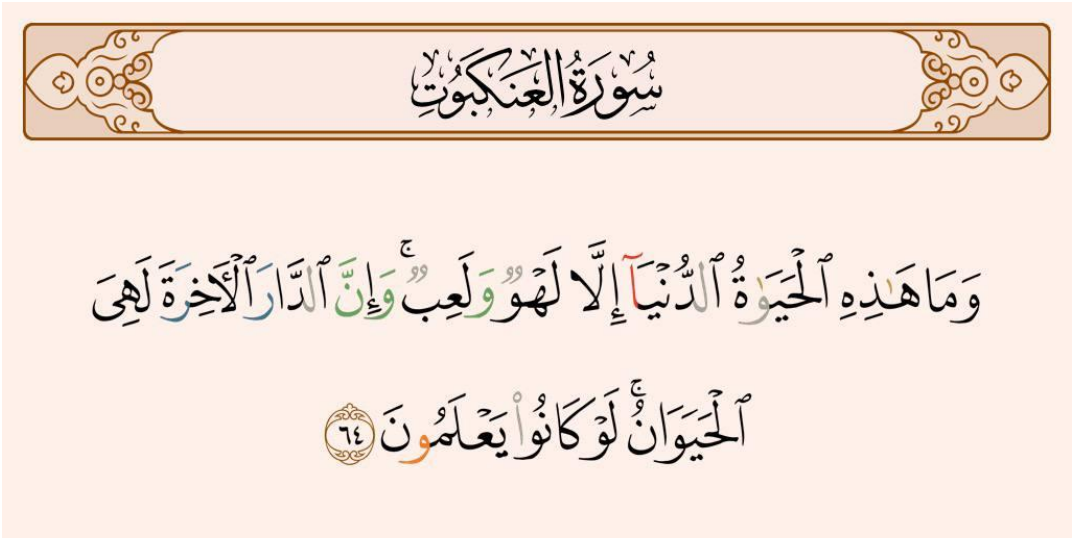
EMBRYOLOGY QUIZ LECTURE 2

External Resources

https://aneskey.com/the-foregut-and-chest-2/

رسالة من الفريق العلمي

اللهم إن عمر عطية في ذمتك وحبل جوارك، فقِه من فتنة القبر وعذاب النار، أنت أهل الوفاء والحق، فاغفر له وارحمه إنك أنت الغفور الرحيم.



وما هذه الحياة الدنيا إلا لهو ولعب، تلهو بها القلوب وتلعب بها الأبدان؛ بسبب ما فيها من الزينة والشهوات، ثم تزول سريعًا، وإن الدار الآخرة لهي الحياة الحقيقية الدائمة التي لا موت فيها، لو كان الناس يعلمون ذلك لما آثروا دار الفناء على دار البقاء.

(التفسير الميّسر)

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Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			