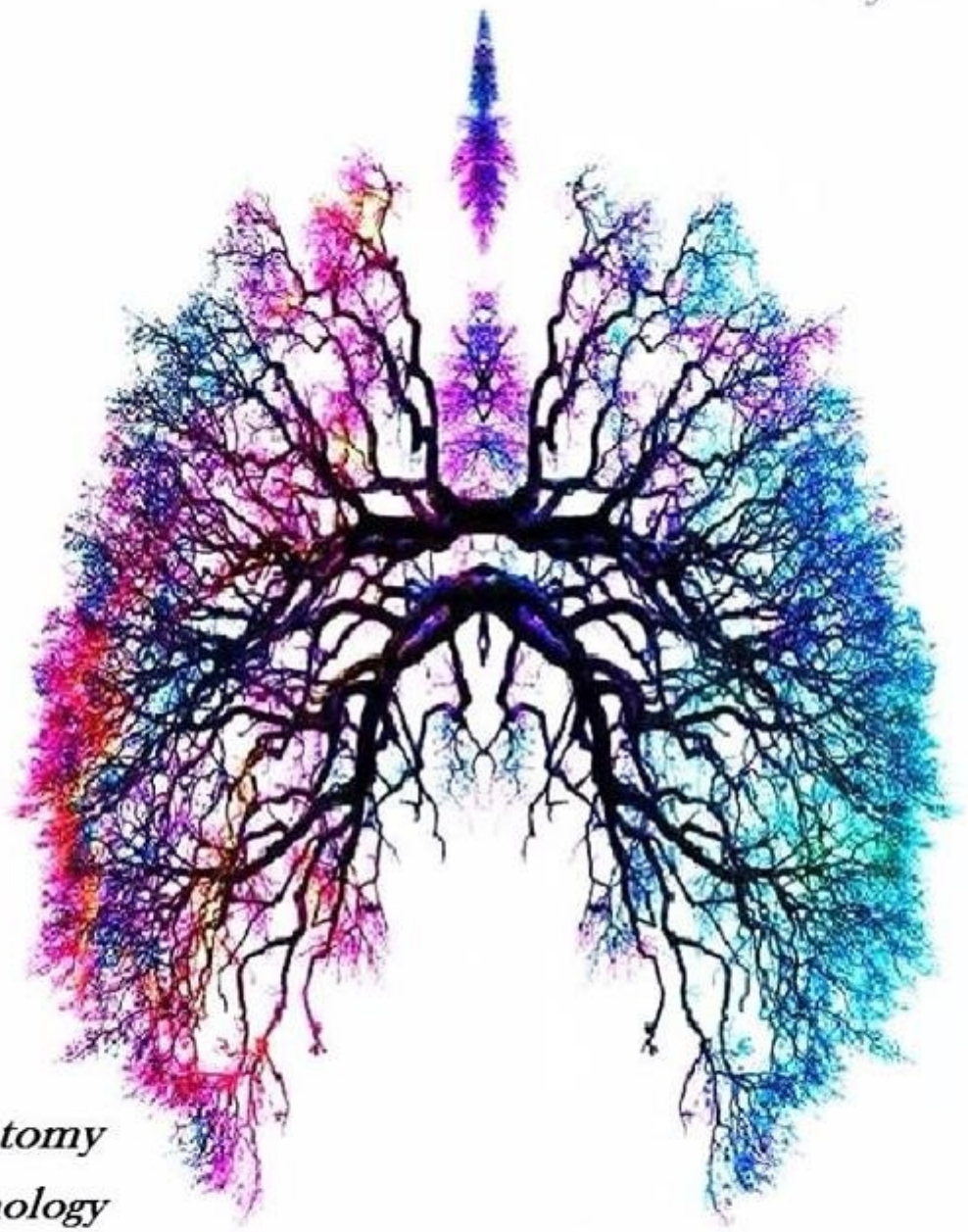
RESPIRATORY SYSTEM

Cover by: Aseil Khatib



- ○ Anatomy
- ○ Pathology
- ○ Physiology
- ○ Pharmacology
- ○ Microbiology
- ○ PBL
- ● Embryology

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Lecture # 2
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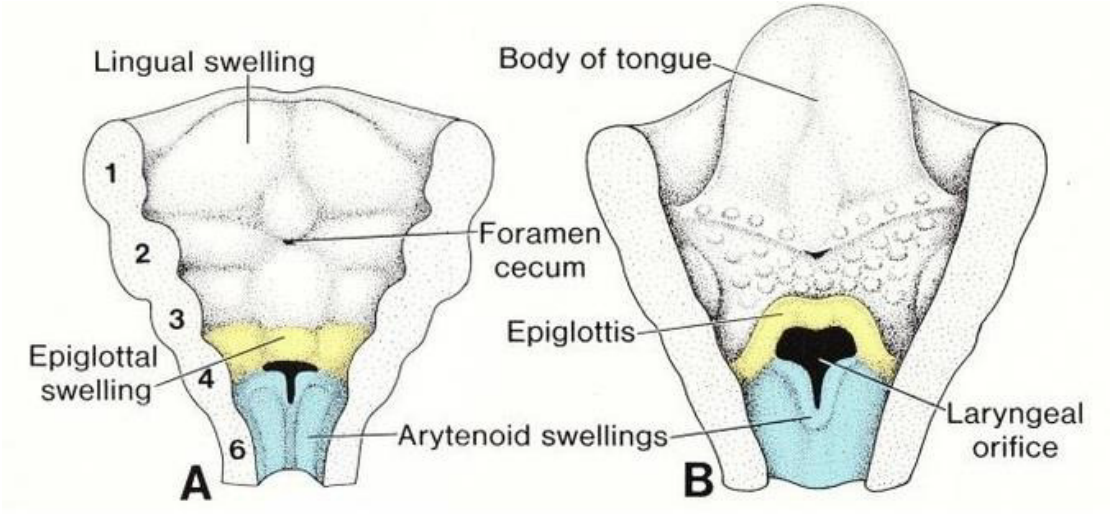
Respiratory System Embryology-2

Larynx:

The wall of the laryngeal cavity consists of lining mucosa, cartilage, ligaments, and muscles and covered exteriorly by connective tissue.

The **internal lining** (epithelium) of the larynx originates from **endoderm**, but the **cartilages, muscles and connective tissue** originate from **mesenchyme (mesoderm**) of the **fourth and sixth pharyngeal arches.** The laryngeal orifice; a communication with the pharynx (nasopharynx according to the doctor), changes in appearance from a slit like opening to a T-shaped opening. (Figure A)



Epiglottal swelling is located above laryngeal orifice (Figure A).

Subsequently, when mesenchyme of the two arches (4^{th}-6^{th}) transforms into the **thyroid, cricoid**, and **arytenoid cartilages**, the characteristic adult shape of the laryngeal orifice can be recognized. (Figure B)

At about the same time, the laryngeal epithelium, preceded by the mesenchyme, proliferates rapidly resulting in temporary occlusion in the lumen of the larynx. This is directly followed by vacuolization and recanalization that produce a pair of lateral recesses, **the laryngeal ventricles**. These recesses are bounded by folds of tissue that differentiate into the **false** (above) and **true** (below) **vocal cords**. This process is essential for ventricle development.

Musculature of the larynx is derived from mesenchyme of the fourth and sixth pharyngeal arches; all laryngeal muscles are innervated by branches of the tenth cranial nerve, the **vagus nerve.**

The **superior laryngeal** nerve innervates derivatives of the **fourth** pharyngeal arch; cricothyroid muscle through its external branch and the **recurrent laryngeal nerve** innervates derivatives of the **sixth** pharyngeal arch (the remaining muscles).

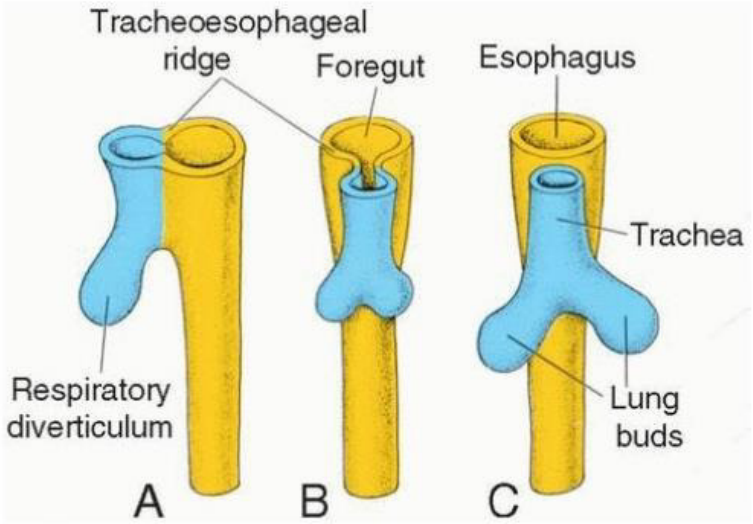
Larynx Anomalies:

- Laryngeal atresia (congenital high airway obstruction syndrome/chaos):

Narrowing or complete obstruction of the larynx. Distal to the atresia or stenosis, dilatation will ensue especially in the lungs which affects the diaphragm causing it to be either flattened or inverted and can lead to fetal ascites (accumulation of fluid in the abdomen) that might be accompanied by accumulation of serous fluid in the chest. Prenatal ultrasonography permits diagnosis. (It mainly refers to obstruction rather than stenosis)

Trachea, Bronchi, and Lungs:

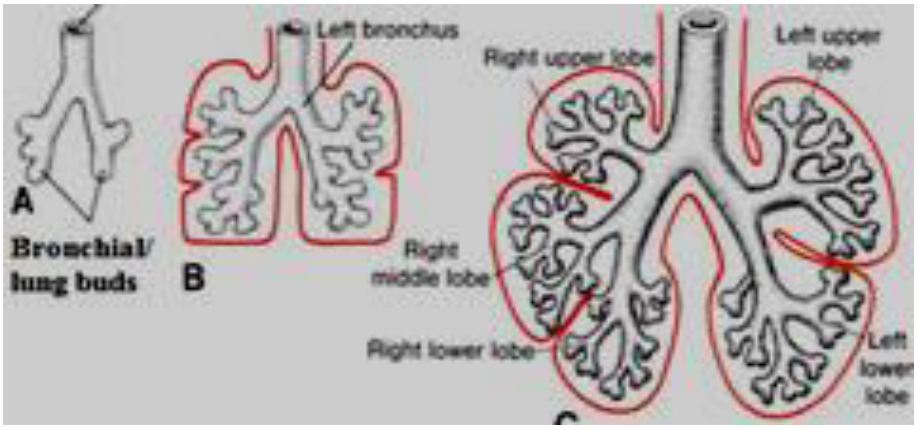
During its separation from the foregut, the **lung bud (**also called tracheal bud or respiratory bud) forms the trachea and two lateral outpocketings, the **bronchial buds.**



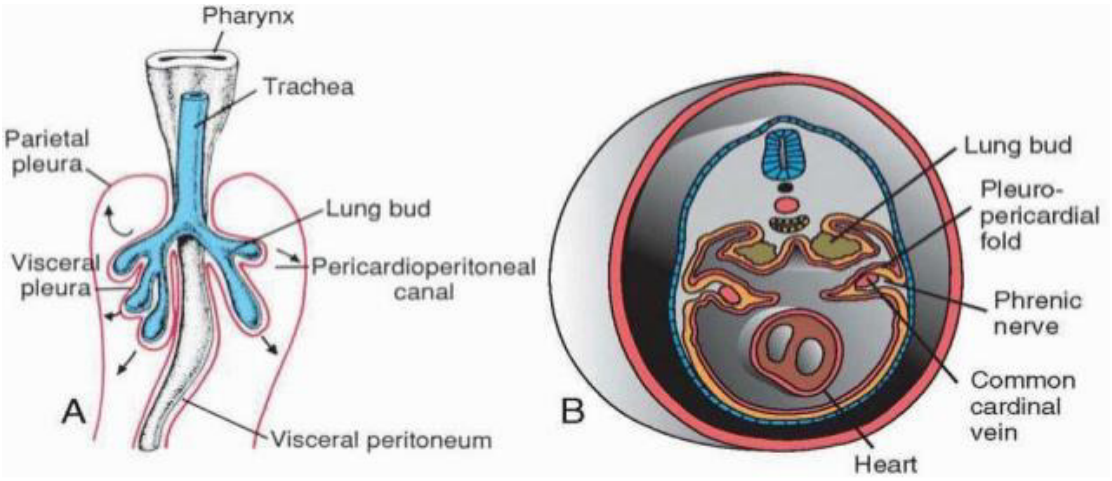
Each of these two buds will enlarge and deviate either to the left or to the right giving rise to the right and left main bronchi. The right then forms three secondary bronchi, and the left, two, thus foreshadowing the three lobes on the right side and

two on the left. 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.

N.B: The left lung consists of 8 segments due to the union of the apicoposterior segments in the superior lobe and the anteromedial segments in the inferior lobe. (These segments will separate after birth giving rise to 10 segments).



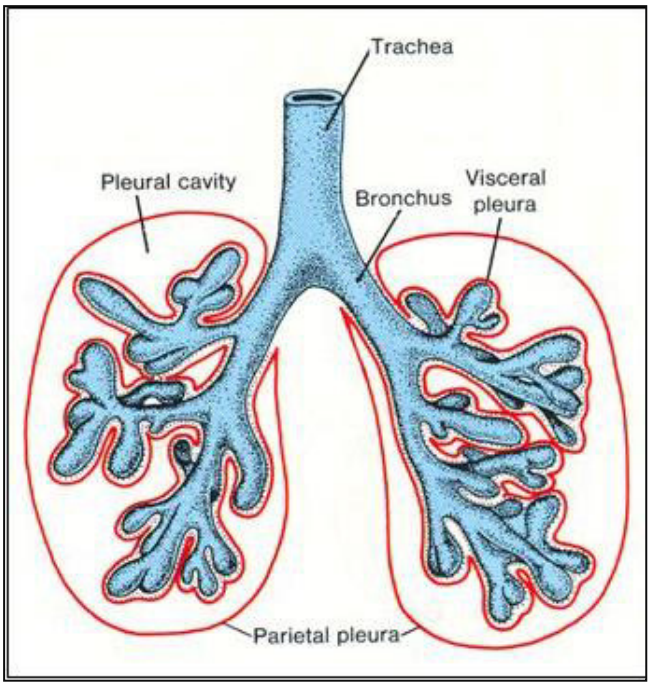
During the growth of the bronchial tree in caudal and lateral directions, the lung buds expand into the body cavity. The spaces for the lungs, **the pericardioperitoneal canals**, are narrow. They lie on each side of the foregut and are gradually filled by the expanding lung buds.



- Expansion of the lung buds into the pericardioperitoneal canals. At this stage, the canals are in communication with the peritoneal and pericardial cavities.
- A. Ventral view of lung buds.
- B. Transverse section through the lung buds showing the pleuropericardial folds that will divide the thoracic portion of the body cavity into the pleural and pericardial cavities.

N.B: The pericardioperitoneal canal will be partitioned into pericardial and peritoneal cavities. The pleuroperitoneal space will be formed after the pericardioperitoneal canal and will give rise to the pleural and peritoneal spaces. (Not shown in the figures).

The **visceral** pleura is derived from the **splanchnic mesoderm** while the **parietal** pleura, covering the thoracic cage, is derived from the **somatic mesoderm**. The space between the parietal and visceral pleura is the pleural cavity. The visceral pleura extends between the lobes of the lungs.



By the end of the sixth month, approximately 17 generations of subdivisions have formed in a dichotomous fashion (1>>2 then 2>> 4 then 4 >>8 …etc). Before the bronchial tree reaches its final shape, however, **an additional 6 division's form during postnatal life.** So, the human respiratory tree may consist on average of 23 generations. (The bronchial or respiratory tree includes all the airway branches from the trachea till the alveoli)

By default, these divisions will give rise to terminal bronchioles, respiratory bronchioles, alveolar ducts, alveolar sacs and alveoli; as we care mostly about the alveoli because it's the principal site of gas exchange and surfactant production.

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 to the fourth thoracic vertebra.

Maturation of the Lungs (Important):

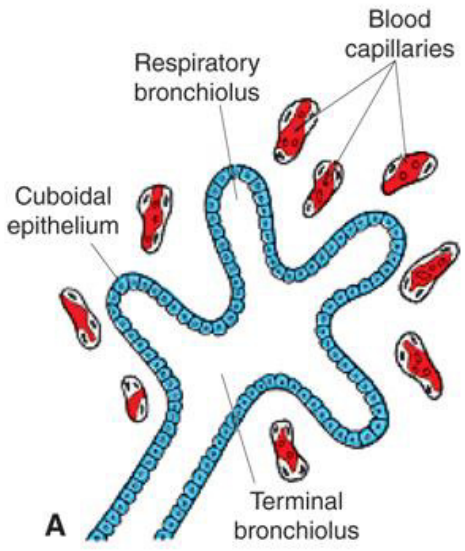
This process is divided into four temporal periods:

Period	Duration	Bronchial tree changes
1- Pseudoglandular period	5/6-16wk (4mth)	Branching has continued to form terminal bronchioles. No respiratory bronchioles or alveoli. **Only simple cuboidal epithelium is present. No respiration**
2- Canalicular period	16-26wk (4-6mth)	Each terminal bronchiole divides into two or more respiratory bronchioles which in turn divide into three or six alveolar ducts. Simple squamous cells could be present, respiration **may** occur.
3- Terminal sac period	26 wk to birth (6mth-end 9mth)	Terminal sacs **(primitive alveoli)** form, and capillaries establish close contact. Since there are simple squamous epithelial cells, **normal respiration is definite if the surfactant amount is sufficient.**
4- Alveolar period **(POSTNATAL)**	8mth to childhood (10 yrs)	Mature alveoli have well developed epithelial endothelial (capillary) contacts.

Notes:

1- The intimate contact between epithelial and endothelial cells makes up the blood-air barrier (fused basal lamina).

2- **Mature alveoli are not present before birth.** They mature after birth and develop by increasing in number ONLY and not in size. (Important)



A. The canalicular period. Note the cuboidal cells lining the respiratory and terminal bronchiole. There is no close contact between the capillary and epithelial cells.

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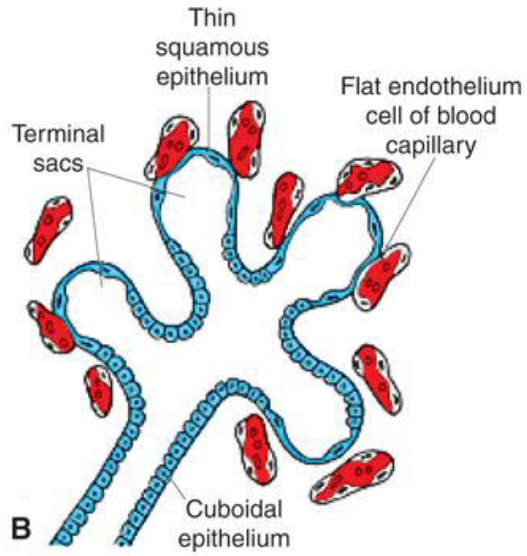
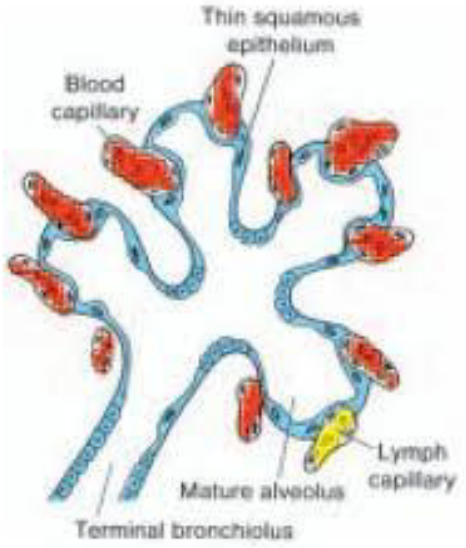


B. Terminal sac period. Cuboidal cells become very thin (simple squamous) and intimately associated with the endothelium of blood capillaries and form terminal sacs (primitive alveoli).



Lung tissue in a newborn. Note the thin squamous epithelial cells (Type I cells) and surrounding capillaries protruding into the alveoli (BAB). Terminal sacs increase.

At the end of the sixth month, type II alveolar cells develop and produce surfactant. The amount of surfactant in the fluid increases particularly during the **last two weeks** before birth.

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).

Fetal **breathing movements begin before birth** and cause aspiration of amniotic fluid. When respiration begins at birth (by tapping the baby on the back to stimulate respiration and she/he cries) 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. The surfactant remains deposited on alveolar cell membranes. Without the fatty surfactant layer, the alveoli would collapse during expiration (atelectasis). This occurs in infant respiratory distress syndrome (IRDS).

Anomalies of the Lung:

1- Infant Respiratory Distress Syndrome (IRDS): (Important)

Previously called hyaline membrane syndrome or hyaline membrane disease, IRDS depends on the amount of surfactant produced. When surfactant is insufficient, the air-water (blood) surface membrane tension becomes high, bringing great risk that alveoli will collapse (atelectasis) during expiration and the syndrome develops. It accounts for approximately **20%** of deaths among newborns.
Intrauterine asphyxia play a role in the development of IRDS by producing irreversible changes in type II cells thus inhibiting surfactant production.
Treatment includes:
Administration of artificial surfactants along with oxygen as well as treatment of **mothers** with premature labor with glucocorticoids (**Betamethazone)**. Nowadays, preterm births in the 6^{th} or 7^{th} months and even 5 moths and a half can be given artificial surfactants, put in an incubator and live normally.
Thyroxin is an important stimulator of surfactant production.

2- Blind- ending trachea with absence and agenesis of single or both lungs.
The trachea won't bifurcate and as result lungs won't form. This is a very rare condition.

3- Abnormal (extra) divisions of the bronchial tree:
The infant will have increased number of lobules and these supernumerary lobules won't affect the respiration but they may cause difficulties during bronchoscopies.

4- Ectopic lung lobe:
Ectopic lung lobes arise from the septum between the trachea and esophagus. It is believed that these accessory lobes are formed from additional respiratory buds that develop independently of the main respiratory system.
They could form in other sites than the chest. (According to the doctor)

5- Congenital cysts of the lung:
They are formed by dilation of terminal or larger bronchi.
These cysts may be small and multiple giving the lung a **honeycomb** appearance on radiograph.
They drain poorly and frequently cause **chronic infections**.

6- Lung hypoplasia:
Lung development is reduced and become smaller in size. It occurs along with **congenital diaphragmatic hernia.** This hernia allows the abdominal viscera to enter the pleural cavity. It is more common on the left side because there is a triangular space (hole-weak point) on the left side which can be penetrated by the abdominal viscera (e.g small intestine). The viscera enter the pleural cavity, compress the lungs and cause hypoplasia. Most infants with CDH die of pulmonary insufficiency as their lungs are too hypoplastic to support life.

Oligohydramnios and Lungs:

Oligohydramnios is a condition in pregnancy characterized by a deficiency of amniotic fluid. It is the opposite of polyhydramnios. When oligohydroamnios is severe, lung development is retarded and severe pulmonary hypoplasia results. This reveals the importance of the amniotic fluid stimulation for the lung development.

- Remember that polyhydramnios is one of the complications of tracheoesophageal fistula.

Final Note:

Fresh and healthy lungs contain some air so pulmonary samples float in water (indicates respiration). The lungs of the stillborn infants are firm and sink in water because they contain fluids not air (indicates lack of respiration). This lung float test helps determine whether or not an infant was stillborn.

"All generalizations are false, including this one"

Best Wishes ☺