



RESPIRATORY BLOCK

Embryology Team Notes

Development of Respiratory System

Student Guide:

- 1- The notes ,which are written by the team , are in **purple** .
- 2- Everything written in **Red** is important.
- 3- Everything written in **Green** is from male slides.
- 4- Everything written in **Pink** is from female slides.

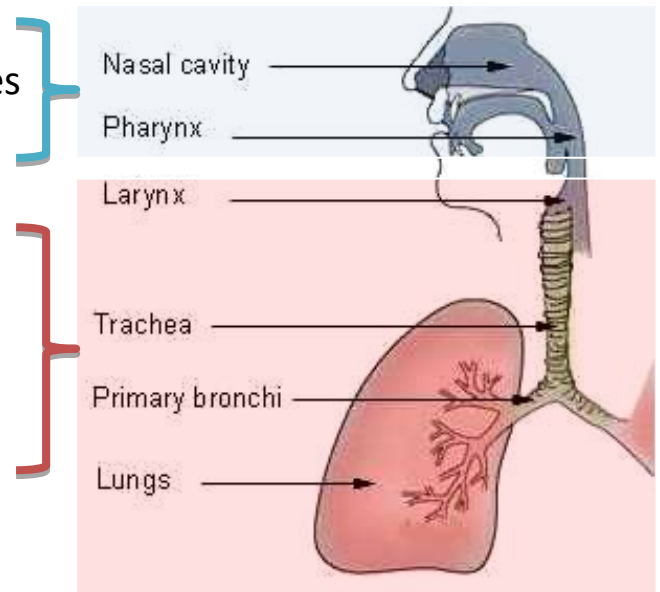
Respiratory System

- Upper respiratory tract:

- ◆ Nose
- ◆ Nasal cavity & paranasal sinuses
- ◆ Pharynx

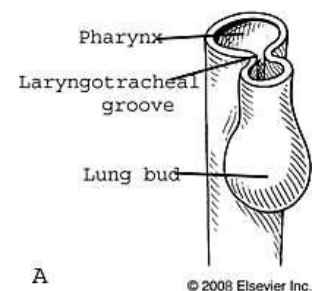
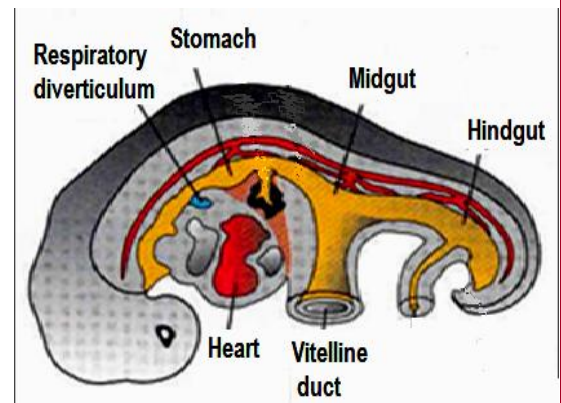
- Lower respiratory tract:

- ◆ Larynx
- ◆ Trachea
- ◆ Bronchi
- ◆ Lungs



Development of the Lower Respiratory Tract

- + Begins to form during the 4th week of development :
 - Begins as a median outgrowth (**laryngotracheal groove**) from the **caudal part** of the **ventral wall** of the **primitive pharynx** .
 - The groove invaginates and forms the **laryngotracheal (respiratory) diverticulum**.



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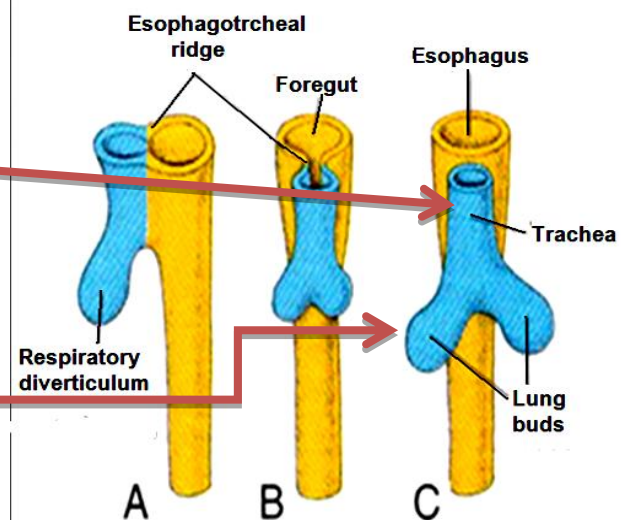
- invaginates = deepens.
- The diverticulum grows in size and becomes surrounded by the splanchnic mesoderm .

A longitudinal tracheo-esophageal septum develops and divides the diverticulum into

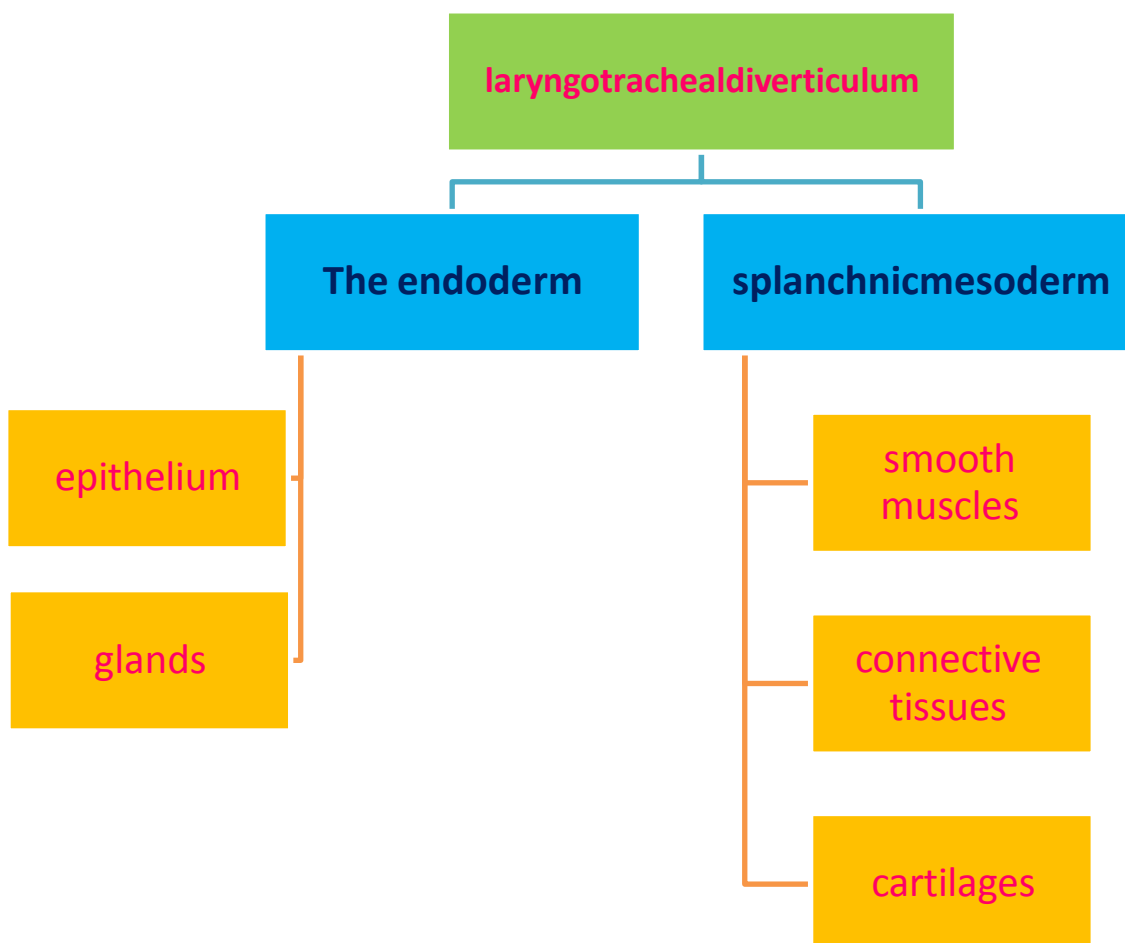
Dorsal portion:
primordium of the
oropharynx and
esophagus

Ventral portion:
primordium of
larynx, trachea,
bronchi and lungs

- The **proximal part** of the respiratory diverticulum remains tubular and forms **trachea**
- The **distal end** of the diverticulum dilates to form **lung bud**, which divides to give rise to **2 lung buds** (primary bronchial buds)



- The **endoderm** lining the **laryngotracheal diverticulum** gives rise to the: **Epithelium & Glands** of the respiratory tract
- The surrounding **splanchnic mesoderm** gives rise to the: **Connective tissue, Cartilage & Smooth muscles** of the respiratory tract



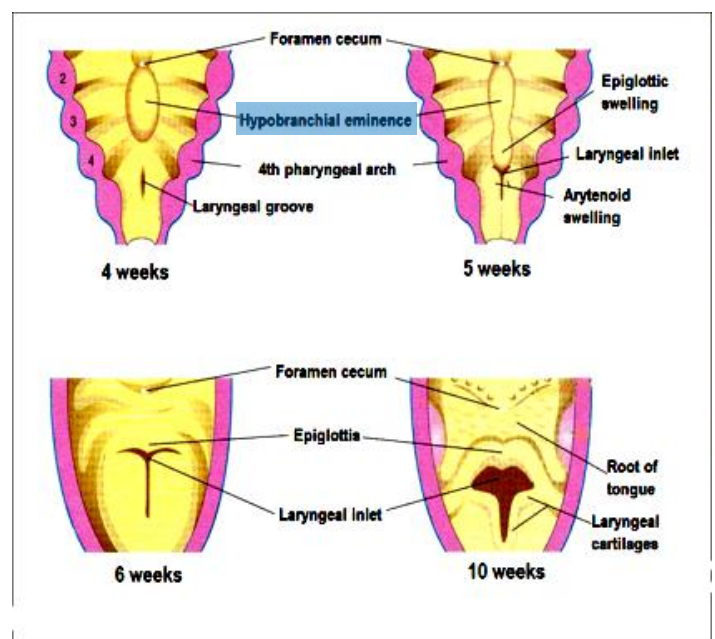
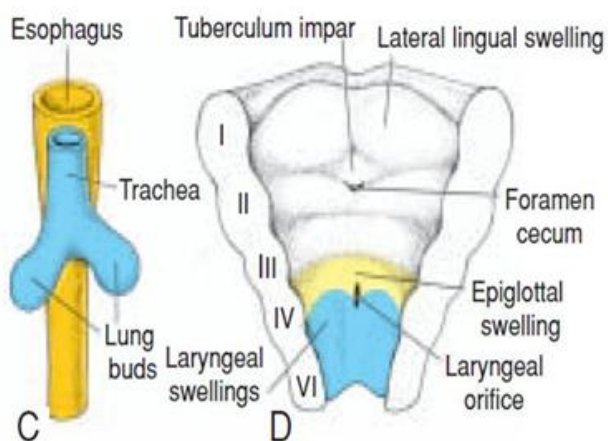
Development of the Larynx

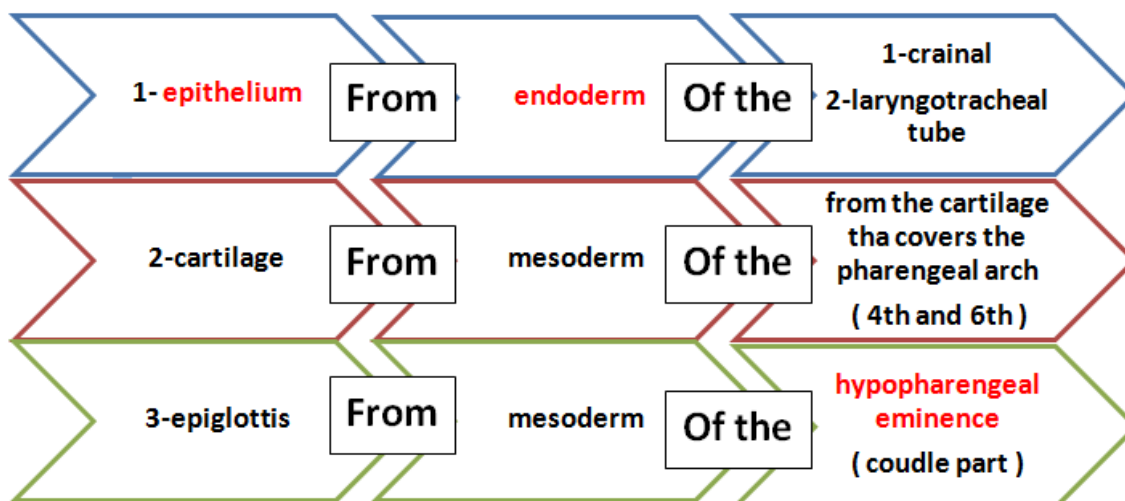
- The opening of the laryngotracheal diverticulum into the primitive foregut becomes the **laryngeal orifice**.
- The **epithelium & glands** are derived from **endoderm**.
- Laryngeal **muscles** & the **cartilages** of the larynx **except Epiglottis**, develop from **the mesoderm** of **4th & 6th** pairs of **pharyngeal arches**.

- Laryngeal orifice = inlet

-The pink part is the pharyngeal arches(as shown below) and it is 6 arches, but we just see 4 arches because the 5th arch maybe absent or only exists transiently during embryological growth and development , and the **4th & 6th arches are fused** together .

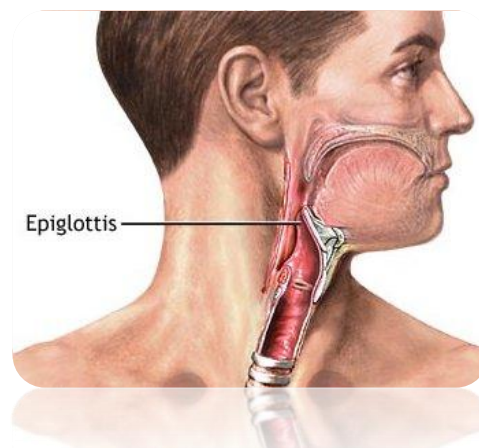
-Epiglottis :The thin elastic cartilaginous structure located at the root of the tongue that folds over the glottis to prevent food and liquid from entering the trachea during the act of .swallowing





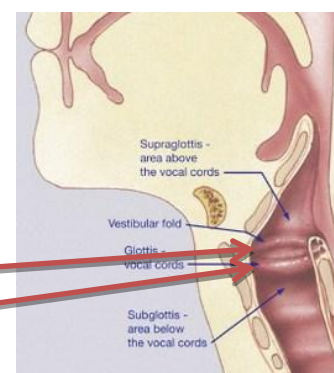
Epiglottis

- It develops from the **caudal part of the hypopharyngeal eminence**, a swelling formed by the proliferation of **mesoderm** in the floor of the pharynx.



Growth of the larynx and epiglottis is rapid during **the first three years** after birth. By this time the epiglottis has reached its adult form.

- The laryngeal epithelium proliferates rapidly resulting in **temporary occlusion** of the laryngeal lumen .
- Recanalization of larynx normally occurs by the **10th week**
- Laryngeal ventricles, **vestibular folds** and **vocal folds** are formed during **recanalization**.

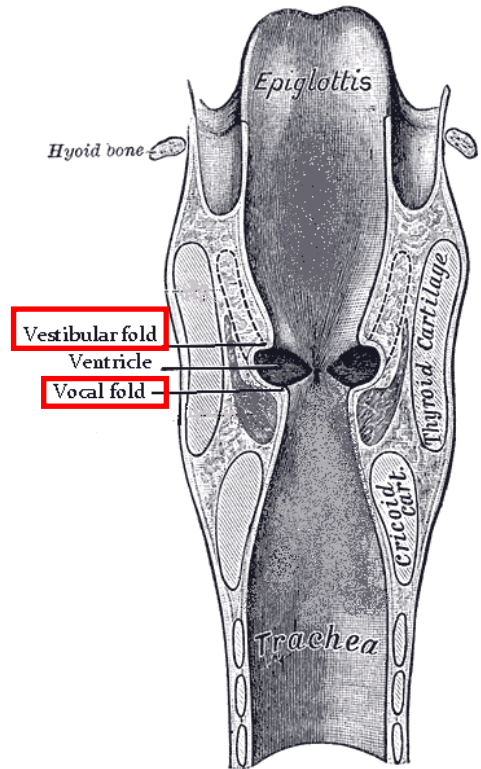


Recanalization = restoration of the channel or by the formation of new channels.

تتحول لأنابيب مفرغة

rapid proliferation of the **laryngeal epithelium** →
temporary occlusion of the laryngeal lumen
 by the 10th week **Recanalization** during it :

- 1- Laryngeal ventricles
- 2- vocal folds
- 3- vestibular folds
(will be formed)



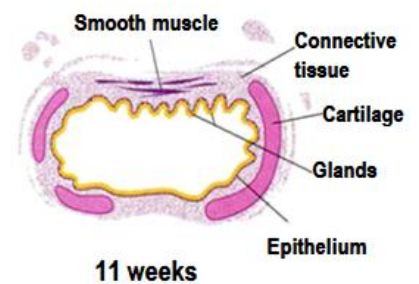
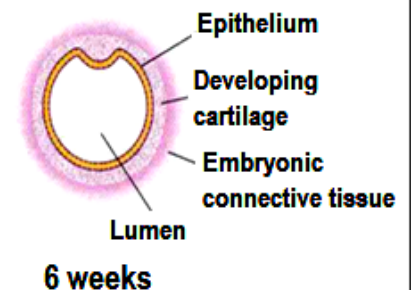
Development of the Trachea

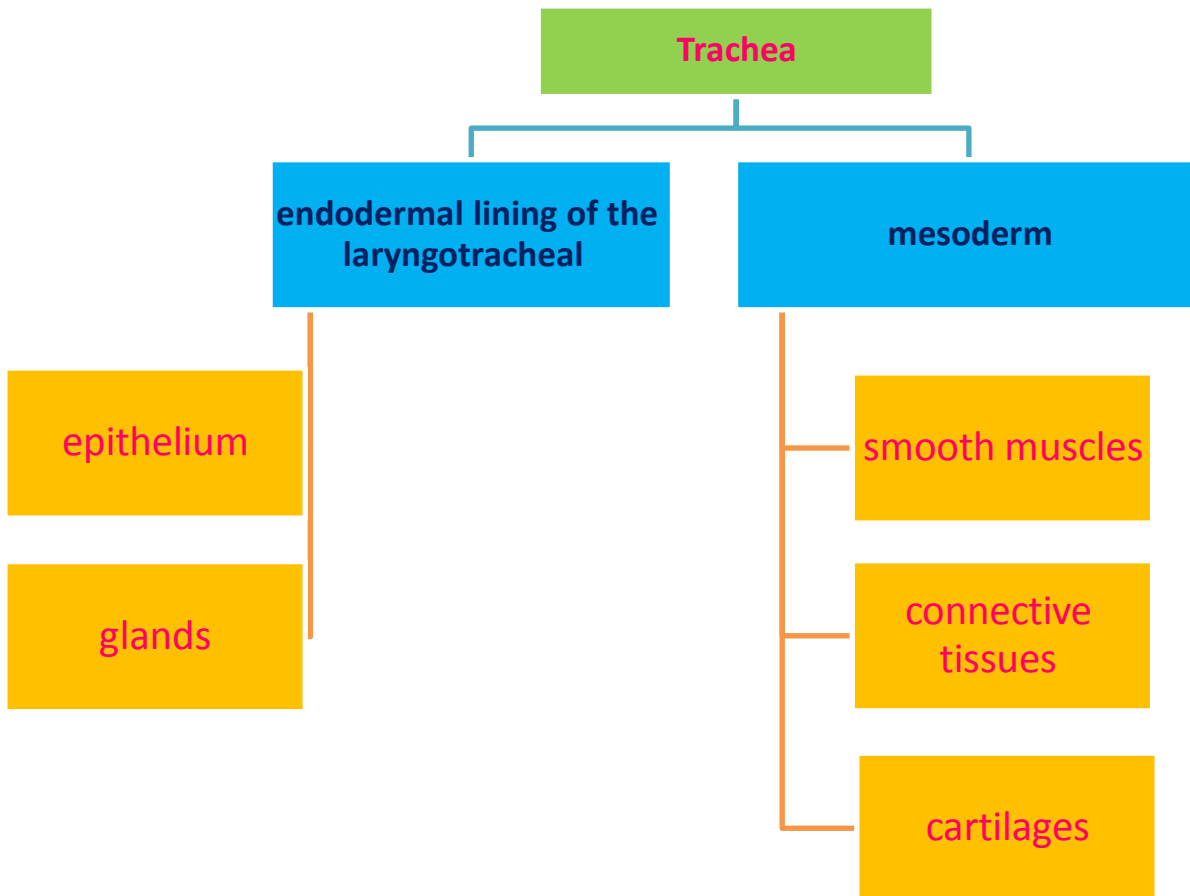
- The **endodermal lining** of the **laryngotracheal tube** distal to the larynx differentiates into the **epithelium and glands** of the trachea and pulmonary epithelium
- The **cartilages, connective tissue,** and **muscles of the trachea** are derived from the **mesoderm**.

So ,

1- the lining will give : epithelium and glands

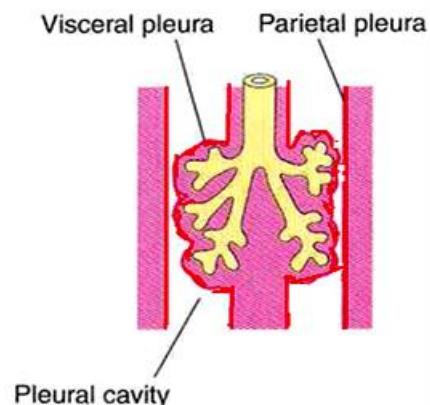
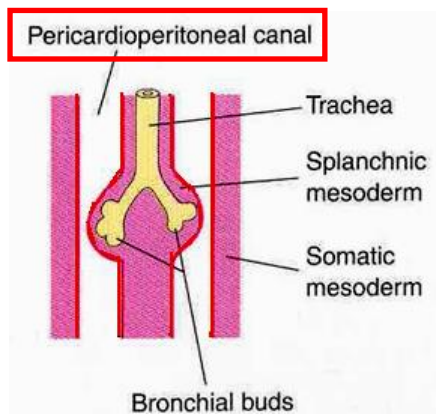
2- the surrounding will give : Cartilages, connective tissue, and muscles



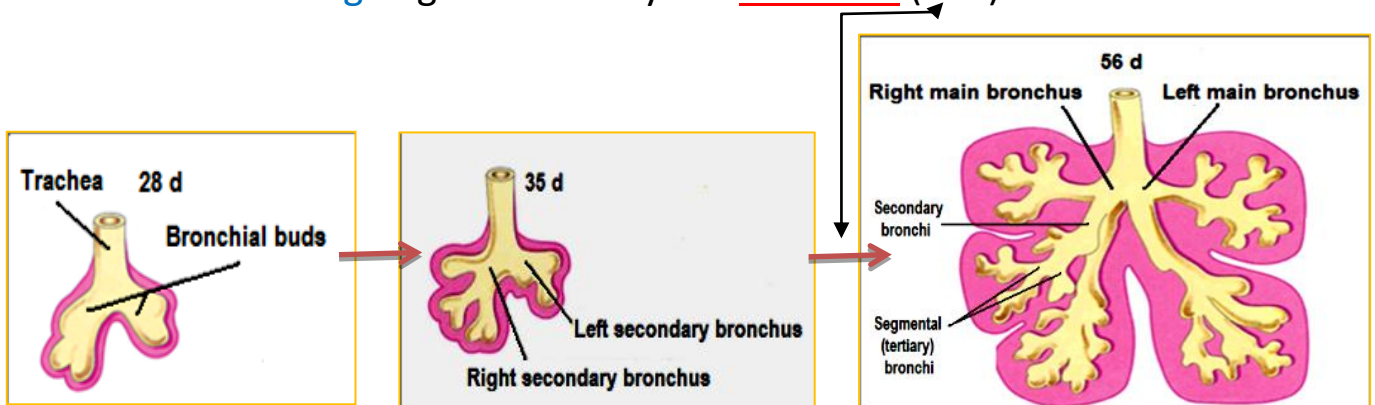


Development of the Bronchi & Lungs

- The 2 primary bronchial buds grow laterally into the **pericardioperitoneal canals** (part of the intraembryonic celome), the primordia of pleural cavities
- **Bronchial buds** divide and redivide to give the **bronchial tree**.



- The **right main bronchus** is slightly **larger** than the left one and is **oriented more vertically**
- The embryonic relationship persists in the adult.
- The **main bronchi** subdivide into **secondary** and **tertiary (segmental)** bronchi which give rise to further branches → **The segmental bronchi will be 10 in right lung and 8 or 9 in the left lung** begin to form by the **7th week (49d)**



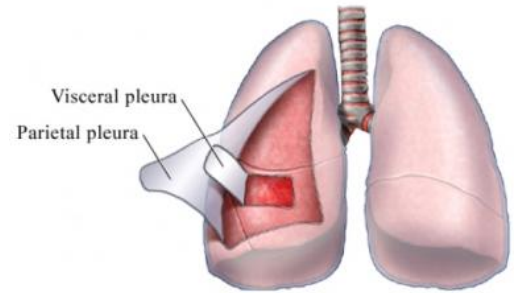
- The surrounding mesenchyme also divides.
- Each segmental bronchus with its surrounding mass of mesenchyme is the primordium of a **bronchopulmonary segment**.

- **Segmental bronchi** numbers are very important
- primordium : an organ or part in the earliest stage of development
- **bronchopulmonary segment** functional and a structural unit

- **By 24 weeks**, about **17 orders of branches** have formed and respiratory bronchioles have developed.
- An additional **seven orders of airways** develop **after birth**.

24 weeks (about 6 months)	17 orders
after birth	7 orders

- As the lungs develop they acquire a layer of **visceral pleura** from splanchnic mesenchyme.
- The thoracic body wall becomes lined by a layer of **parietal pleura** derived from the somatic mesoderm.



- Lung formation doesn't stop at or before the birth , it's continuous until 3- 8 years.
- Splanchnic : any mesoderm covering the viscera.
- Somatic: any mesoderm covering the body wall.

Maturation of the Lungs

✚ **Maturation of lung is divided into 4 periods:**

Very Important

Pseudoglandular
5 - 17 weeks

Canalicular
16 - 25 weeks

Terminal sac
24 weeks - birth

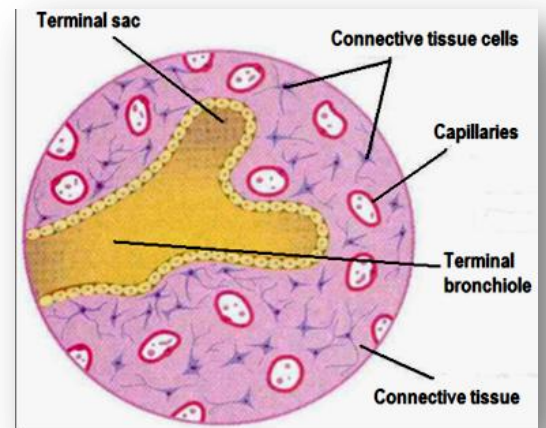
Alveolar
late fetal period -
childhood

- These periods overlap each other because **the cranial segments of the lungs mature faster than the caudal ones.**

1- Pseudoglandular Period (5-17 weeks)

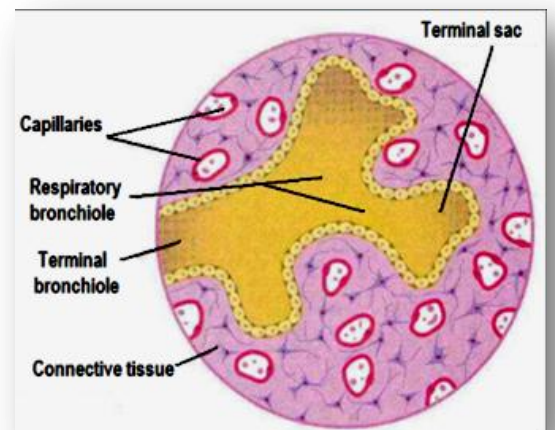
- ✓ Developing lungs somewhat resembles an **exocrine gland** during this period.
- ✓ By **17 weeks** all **major elements** of the lung have formed except those involved with gas exchange.
- ✓ So, Respiration is **NOT** possible
- ✓ **Fetuses born during this period are unable to survive.**

- Respiration is **NOT** possible because there are no alveoli.
- So babies born during the 4th month unable to survive.



2- Canalicular Period (16-25 weeks)

- ✓ Lung tissue becomes **highly vascular**.
- ✓ Lumina of bronchi and terminal bronchioles become larger.
- ✓ By **24 weeks** each **terminal bronchiole** has given rise to two or more **respiratory bronchioles**

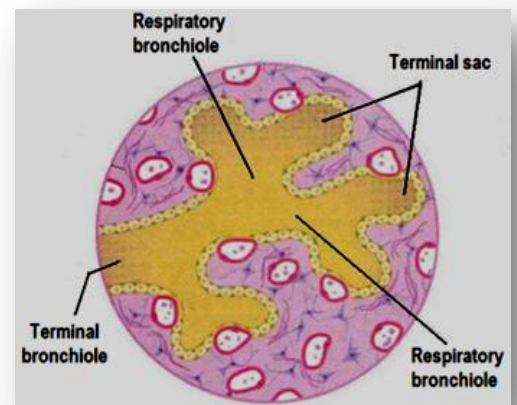


- ✓ The respiratory bronchioles divide into 3 to 6 **tubular passages** called **alveolar ducts**.
- ✓ Some thin-walled **terminal sacs (primordial alveoli)** develop **at the end of respiratory bronchioles**.
- ✓ Respiration **is possible** at the end of this period.
- ✓ Fetus born at the end of this period **may survive** if given **intensive care** (but usually die because of the **immaturity** of respiratory as well as other systems)

- Terminal sac: the alveoli in the future..
- **intensive care** : extensive and continuous care and treatment.

3- Terminal Sac Period (24 weeks - birth)

- ✓ Many more terminal sacs develop.
- ✓ Their **epithelium becomes very thin**.
- ✓ Capillaries begin to bulge into developing alveoli.
- ✓ The **epithelial** cells of the **alveoli** and the **endothelial** cells of the **capillaries** come in intimate contact and establish the **blood-air barrier**. (important)
- ✓ Adequate **gas exchange** can occur which allows the **prematurely** born fetus to survive



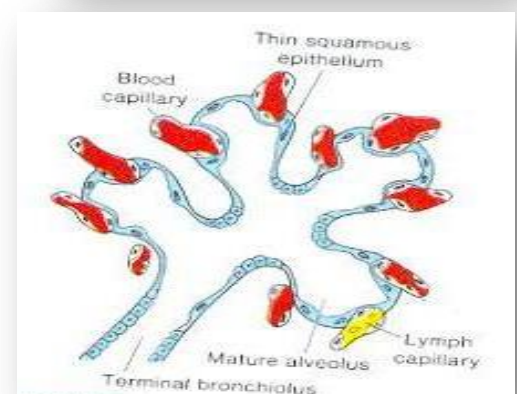
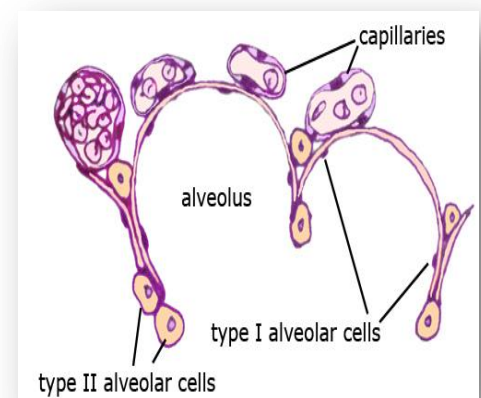
- Bulge into = come in contact = there is gas exchange.
- Respiratory is possible because there is gas exchange .

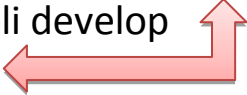
- ✓ By **24 weeks**, the **terminal sacs** are lined by:
 1. Squamous **type I pneumocytes** and
 2. Rounded secretory, **type II pneumocytes**, that secrete a mixture of phospholipids called **surfactant**.

- Surfactant production begins by **20 weeks** and increases during the terminal stages of pregnancy.
- Sufficient **terminal sacs, pulmonary vasculature and surfactant** are present to permit survival of a **prematurely born infants**
- Fetuses born **prematurely at 24-26 weeks** may suffer from **respiratory distress** due to **surfactant deficiency** but may survive if given **intensive care**.

4- Alveolar Period (32 weeks – 8 years)

- ✓ At the beginning of the alveolar period, **each respiratory bronchiole** terminates in a cluster of thin-walled **terminal saccules**, separated from one another by loose connective tissue.
- ✓ These terminal saccules represent **future alveolar sacs**.
- ✓ The epithelial lining of the terminal sacs attenuates to an extremely **thin squamous epithelial** layer.



- Characteristic mature alveoli **do not form until after birth**. 95% of alveoli develop **postnatally**. 
- About 50 million alveoli, one sixth of the adult number are present in the lungs of a **full-term newborn infant**.

- ✓ Most increase in the **size of the lungs** results from an **increase in the number** of respiratory bronchioles and primordial alveoli. rather than from an **increase in the size of the alveoli**.

- From **3-8 year** or so, **the number of immature alveoli continues to increase**. Unlike mature alveoli, **immature alveoli have the potential for forming additional primordial alveoli**.
- By about the **eighth year**, the **adult complement of 300 million** alveoli is present.

Breathing Movements :

- Occur **before birth**, are **not continuous** and **increase as the time of delivery approaches**.
- Help in **conditioning the respiratory muscles**.
- Stimulate **lung development** and are essential for normal lung development.

Lungs at birth :

- The **lungs are half filled** with **fluid derived from the amniotic fluid and from the lungs & tracheal glands**.
- This fluid in the lungs is **cleared at birth**: by:
 - **Pressure on the fetal thorax during delivery**.
 - **Absorption into the pulmonary capillaries and lymphatics**.

Lungs of a Newborn :

- **Fresh healthy lung always contains some air** (lungs float in water).
- **Diseased lung** may contain **some fluid** and may not float (may sink).
- **Lungs of a stillborn infant** are firm, contain fluid and may sink in water.

Factors important for normal lung development :

1 Adequate thoracic space for lung growth.

2 Fetal breathing movements.

3 Adequate amniotic fluid volume.

Developmental anomalies

- Laryngeal tresia.
- **Tracheoesophageal fistula.**
- Tracheal stenosis & atresia.
- Congenital lung cysts.
- Agenesis of lungs.
- Lung hypoplasia.
- Accessory lungs.

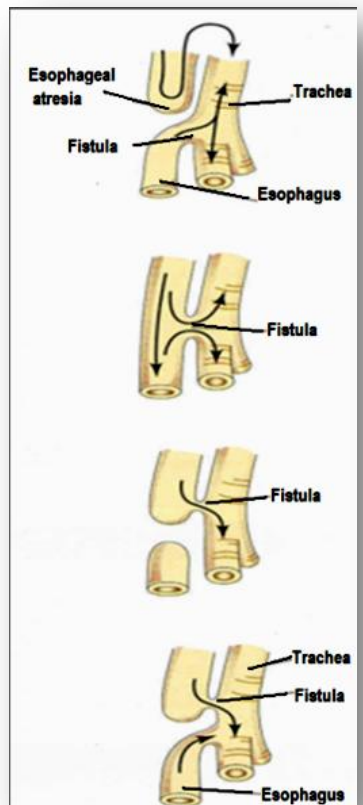
- Atresia : the congenital absence, or the pathological closure, of an opening, passage, or cavity.

- stenosis : a narrowing or stricture of a passage or vessel.

-agenesis : is the absence of the lungs.

Tracheoesophageal Fistula

- An **abnormal passage** between the **trachea and esophagus**.
- Results from **incomplete division** of the cranial part of the foregut into respiratory and esophageal parts.
- Occurs once in 3000 to 4500 live births.
- Most affected infants are **males**.
- In more than **85% of cases**, the fistula is **associated with esophageal atresia**.



Q1- all of the larynx structures are developed from the mesoderm of 4th & 6th pairs of pharyngeal arches except :



1. laryngeal muscles.
2. most cartilages of larynx
3. epiglottis.
4. there is no correct answer.



Q2- maturation of the Terminal sac occur in :

1. Pseudoglandular
2. Canalicular
3. Terminal sac
4. Alveolar



Q3- by the 7th week , how many segmental bronchi in the left lung :

1. 11 or 10
2. 10
3. 9 or 8
4. 7



Q4-Terminal bronchioles give rise to:

1. a)Respiratory bronchioles.
2. b)Terminal sac.
3. c)Alveolar ducts.
4. d)alveoli.



Q5-The right main bronchus is:

1. a)Larger than the left and oriented less vertically.
2. b)Larger than the left and oriented more vertically.
3. c)Smaller than the left and oriented less vertically.
4. d)Smaller than the left and oriented more vertically.

Time	Events
<p style="text-align: center;">Forth week</p>	<ul style="list-style-type: none"> *Starting development of the lower respiratory system at the laryngotracheal groove. *laryngotracheal groove deepens to produce laryngotracheal diverticulum. *separation of laryngotracheal diverticulum by development of tracheoesophageal septum. *The proximal part of the respiratory diverticulum forms the trachea. * The diverticulum develops a lung bud at its distal end. *development of epithelium & glands of larynx from the endoderm. *development of muscles & cartilages of larynx (except epiglottis) from the mesoderm of 4th & 6th pairs of pharyngeal arches.
<p style="text-align: center;">fifth week</p>	<ul style="list-style-type: none"> *the lung bud divides into two bronchial buds. *development of epiglottis from hypopharyngeal eminence. *initiation of pseudoglandular period.
<p style="text-align: center;">Seventh week</p>	<ul style="list-style-type: none"> *10 segmental bronchi in right lung and 8 or 9 segmental bronchi in the left lung begin to form.
<p style="text-align: center;">Eight week and ninth week</p>	<p>Temporarily occlusion begins</p>
<p style="text-align: center;">Tenth week</p>	<ul style="list-style-type: none"> *recanalization of larynx.
<p style="text-align: center;">16 weeks</p>	<ul style="list-style-type: none"> *initiation of canalicular period.

17 weeks	*all major elements of the lung (bronchi & terminal bronchi) have formed <u>except</u> those involved with gas exchange (pseudoglandular period).
20 weeks	*starting production of surfactant which increases during the terminal stages of pregnancy (terminal sac period).
24 weeks	17 order of lung branches is formed .
25 weeks	*termination of canalicular period.
32 weeks	*initiation of alveolar period.
At birth	*termination of terminal sac period. *the fluid of lung is cleared.
After birth	*rapid growth of larynx & epiglottis exactly at the first three years (by this time epiglottis has reached its adult form). *development of additional seven orders of airways. *formation of characteristic mature alveoli and 95% of alveoli will develop. * The number of immature alveoli continues to increase (3-8 years). *the adult complement of 300 million alveoli is present (8 years). *termination of alveolar period.