RS Embryology

DOCTOR NOTES
LECTURE NO.1+2

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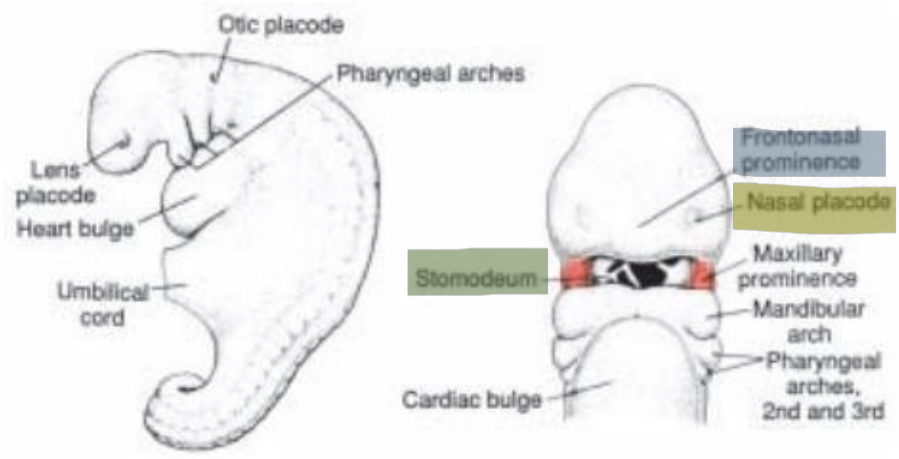
Development of the RS



Placode= site of organ development. For example: Otic placode: beginning of the ear, Lens placode: beginning of the eye…

Prominence: site of area development

*prominence indicates the proliferation of cells after a certain stimulus.

Stomodeum: the anterior part of the oral cavity (we will need this when we talk about the palate which divides between the oral and nasal cavities)

Development of the Nose:

To understand the embryology of the nose we need to remember its anatomy.
It has two anterior openings, and two posterior ones (choanae). It has 2 cavities with a septum in between. So how do these structures form?

Overview:

- ✓ The development starts from the nasal placode and it makes the first part of nasal opening (nostrils). Nostrils are the beginning of nasal cavity —> the vestibules.
- ✓ At the end of the fourth week, facial prominences consisting primarily of neural crest-derived mesenchyme appear. Frontonasal prominence begins from frontal bone descending to the nose forming the septum of the nose.

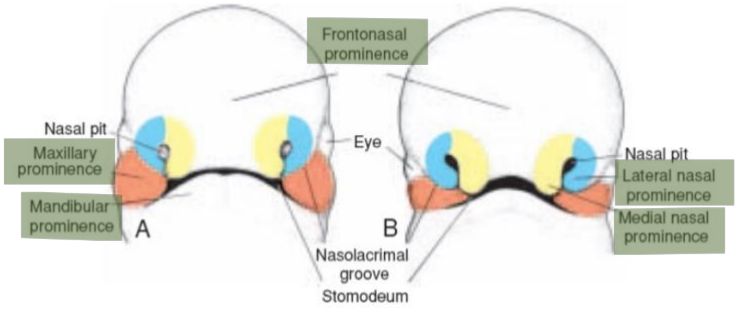
Details:

• During the fifth week of pregnancy, the nasal placodes invaginate to form nasal pits/openings (nostril), they are made up of skin (ectodermal origin).

Then the invagination of cells gives vestibules (a dilatation). In so doing, they create a ridge of tissue that surrounds each pit and forms the nasal prominences.

*remember that the lining epithelium of vestibule is stratified squamous keratinized (skin)

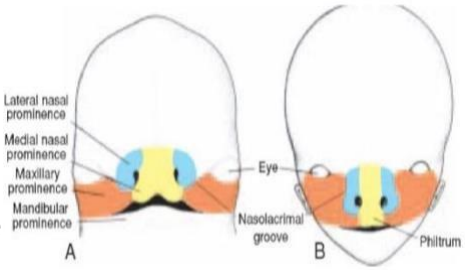
• The prominences on the outer edge of the pits are the **lateral nasal prominences**; those on the inner edge are the **medial nasal prominences.**



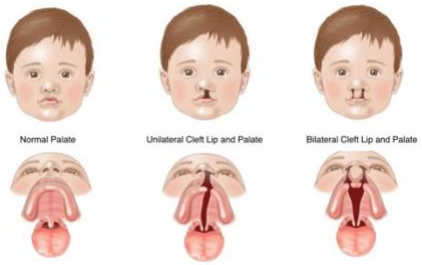
*We can tell that the lateral prominences will make the lateral nasal wall and that the medial prominences (with the frontonasal prominence) will make the septum.

• Maxillary prominence (maxilla, upper jaw) participates in forming the upper lip and nose.
• Mandibular prominence (mandible, lower jaw).

• During the following 2 weeks (6th & 7th weeks), the maxillary prominences continue to increase in size medially.
• The medial nasal prominence is predominant in the midline.
• Maxillary prominences grow medially, compressing the medial nasal prominences toward midline.



• The 2 medial nasal prominences meet to make the philtrum. And they fuse with the frontonasal prominence above to make the septum.
• Subsequently the cleft between the medial nasal prominence and the maxillary prominence is lost, and the two fuse.
Remember from GI: if this fusion is defected, the baby is born with a cleft lip.
(Unilteral or bilateral, with or without a cleft palate)



Medial nasal prominence gives:

1. tip of the nose
2. Septum
3. medial part of upper lip (philtrum).

Extra pic

To summarize: the nose is formed from five facial prominences:

• the frontal prominence gives rise to the nasal septum
• the merged medial nasal prominences provide the crest and tip of the nose
• the lateral nasal prominences form the sides (alae) and lateral wall
• nasal placode forms the nostril and then becomes deeper to form the vestibule

TABLE 15.2 Structures Contributing to Formation of the Face

Prominence	Structures Formed
Frontonasal[a]	Forehead, bridge of nose, medial and lateral nasal prominences
Maxillary	Cheeks, lateral portion of upper lip
Medial nasal	Philtrum of upper lip, crest and tip of nose
Lateral nasal	Alae of nose
Mandibular	Lower lip

And lateral wall

And lower mandible

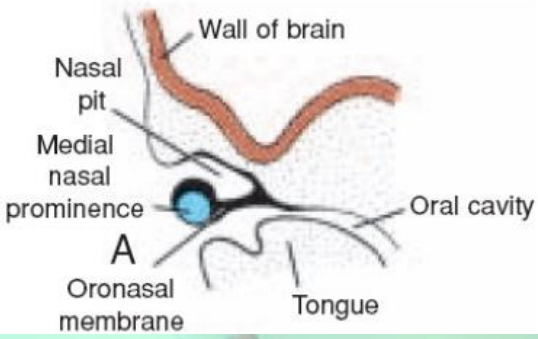
[a] The frontonasal prominence is a sin … he other prominences are paired.

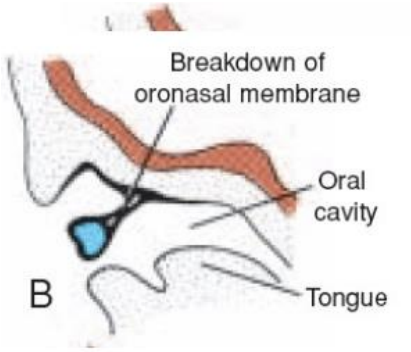
Nasal cavities

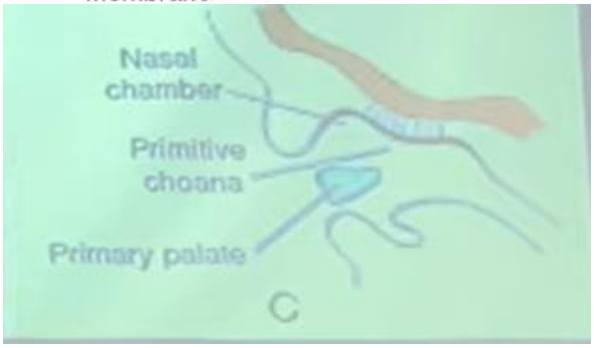
Now invagination and proliferation of nasal prominences will take place to form the cavities.

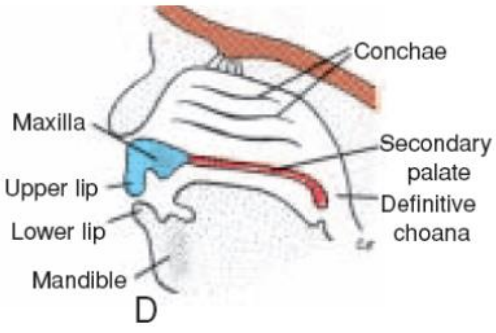
(Compare sentence to related pic below)

A. During the sixth week, the nasal pits invaginates into the underlying mesenchyme, forming the nasal cavity
B. The oronasal membrane is in the position of the hard palate which separates the oral cavity from the nasal cavity. (oronasal membrane ruptures/breaks down aiding to form the primary palate—> secondary palate).
C. The primitive choanae is formed (postrior nares).
It only develops when the membrane forms so the oral and nasal cavities are separated by the primary palate.
D. Later, with formation of the secondary palate, the definitive choanae will appear and open into the nasopharynx.
E. Oral and nasal cavities are separated









Paranasal air sinuses

They are cavities in the skull bone.

Each sinus has a duct opening in the lateral wall of the nose.

Paranasal air sinuses develop as diverticula of the lateral nasal wall and extend into the maxilla, ethmoid, frontal, and sphenoid bones.

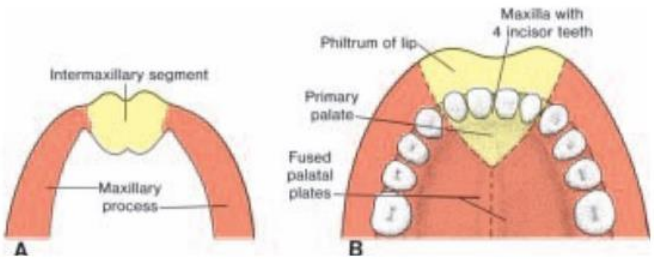
In the development, the prolifiration begins from the opening of the lateral wall of the nose. Invagination in mesenchymal cells backwards and upwards form a cavity reaching cranial bones.

Sinuses are very small in size at the beginning, but with the development of the face at puberty, Paranasal sinuses reach their adult size.

Primary palate

Intermaxillary segment

a structure formed when the two Maxillary prominences grow towards the midline merge and fuse with the medial nasal prominence. (Medial nasal prominence plays a bigger role)



It forms:

1. Labial component: Philtrum of the upper lip
2. Upper jaw component, which carries the four incisor teeth
3. Palatal component, which forms the triangular primary palate

*The frontonasal prominence grows forwards and downwards to reach the intermaxillary segment at the primary palate. (For full separation of the 2 cavities of the nose)

As a summary, the primary palate:

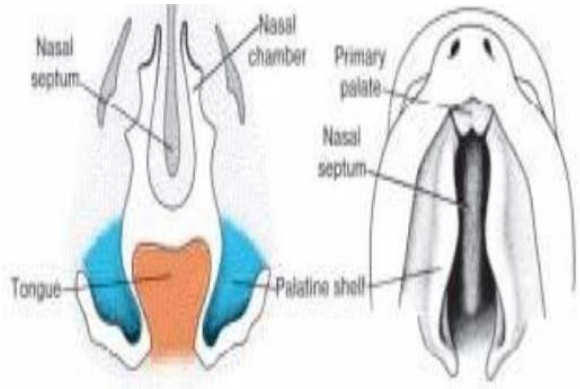
1. Formed by intermaxillary segment
2. Triangular in shape
3. Meets the frontonasal prominence

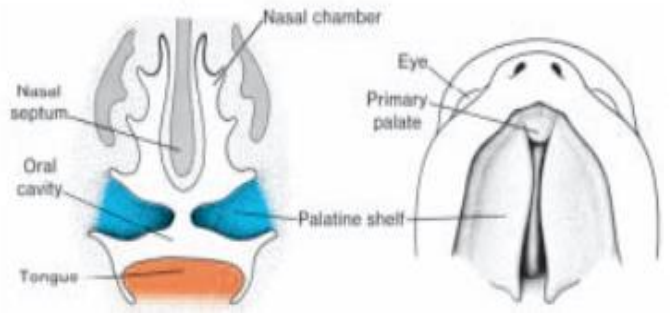
Secondary Palate

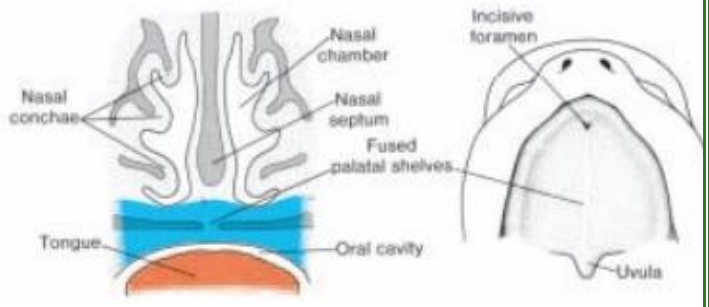
Secondary palate is primarily formed by the **palatine shelves:**

- ✓ two outgrowths from the lateral side of the maxilla.
- ✓ They appear in the sixth week
- ✓ directed obliquely, medially and downwards on each side of the tongue -to reach the 1ry palat, forming the hard palate.
- ✓ In the 7th week the shelves fuse forming the 2ry palate.

*Incisive foramen is positioned between the 1ry and 2ry palates. From this foramen, an artery and nerve enter to supply the nose.







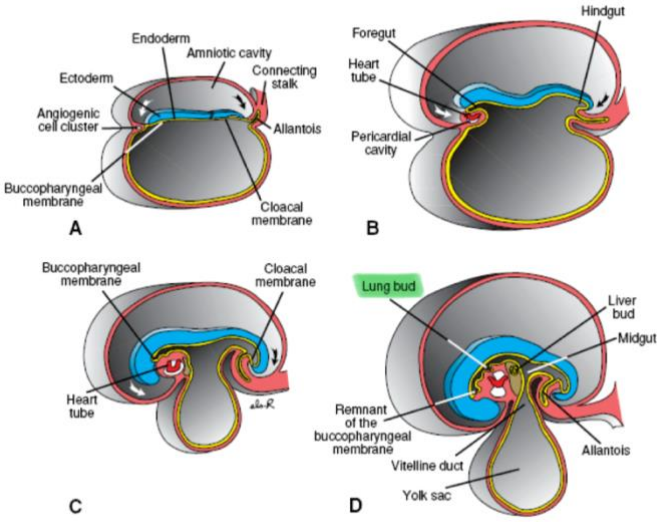
- ✓ They also fuse with the nasal septum which makes the 2 cavities of the nose
- ✓ They also grow posteriorly from the edge of palatine processes to form:
  1. Soft palate
  2. Uvula
     - The union of the 2 folds of the soft palate occurs during the 8th week
     - The 2 parts of the uvula fuse in the midline during the 11th week

*sometimes you look at the uvula and find a cleft in the midline which indicates incomplete fusion of the 2 parts.

Unilateral cleft lip can extend to the nose, (a cleft lip might be unilateral or bilateral/ complete or incomplete).

Development of the Respiratory System

Picture color reference: yellow: endoderm, blue: ectoderm, red: mesoderm)



- The development of the respiratory system begins at the 4th week of embryonic life.
- The respiratory bud and primitive gut are the markers for genesis of the respiratory system.
- The gut tube is divided into four parts, each contributing to different structures:

1. Pharyngeal gut

- Extends from the posterior part of the oral cavity to the pharynx.
- remember that the pharynx is derived from the pharyngeal arches

2. Foregut

- Extends from the lower part of the esophagus to the stomach and the proximal half of the duodenum
- Includes the second part of the duodenum, where the liver bud forms as an outgrowth

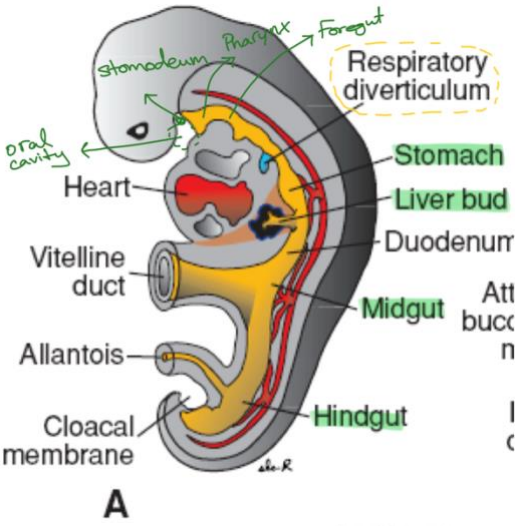
3. Midgut

- Includes the small intestine and the large intestine up to the lateral third of the medial two-thirds of the transverse colon

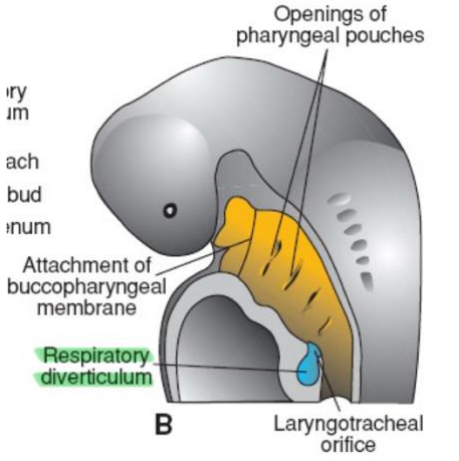
4. Hindgut

- Extends from the lateral third of the transverse colon to the descending colon, sigmoid colon, and anal canal.

Development of the Respiratory Bud

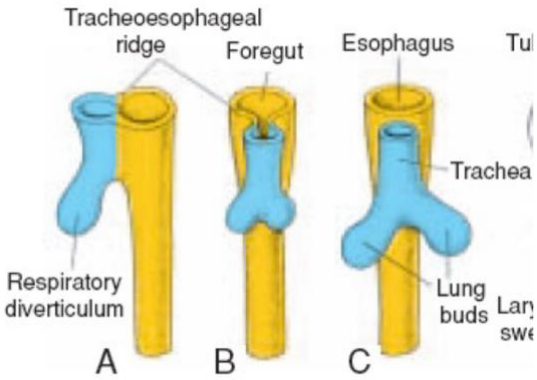


- The respiratory bud, also known as the respiratory diverticulum or lung bud, is the origin of the entire respiratory tract. Check its position in the pic.
  *the Dr talked briefly about the hindgut and midgut, info which we've taken before and are not the focus of this lecture.
- It forms during the 4th week of embryonic development as an outgrowth from the ventral wall of the foregut.
- During the 4th week the bud is **stimulated** so the outgrowth of cells begins, signaling the development of the respiratory tract.
- Tissue Derivatives:
  - The lining epithelium of the respiratory tract is derived from the endoderm.
  - The cartilage, connective tissue, and muscles of the respiratory system arise from the splanchnic mesoderm (mesenchymal cells)



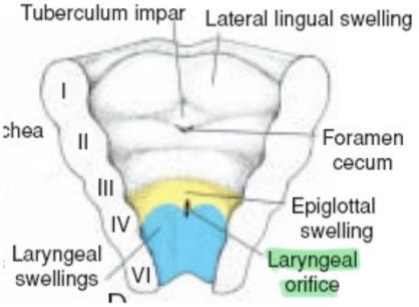
- Connection to the Foregut:

Initially, the respiratory diverticulum is connected to the foregut. However, this connection needs to be separated. Two tracheoesophegeal ridges form, one on each side of the diverticulum. Then they fuse to form the tracheoesophegeal septum. It is a complete septum which divides the forgut into a dorsal portion, the esophagus (digestive tract), and a ventral portion, the trachea and lung buds (respiratory tract).



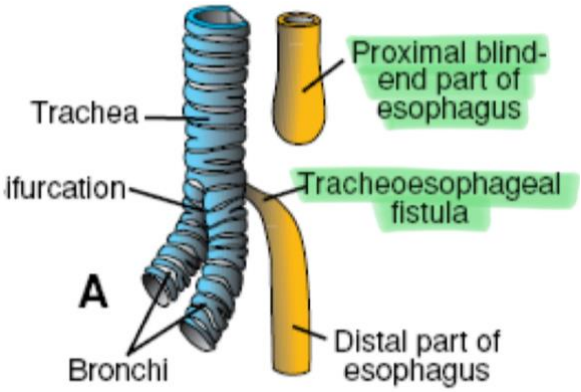
As we know, the inlet of larynx is the connection between the RT and the GIT.
Developmental Connection: larynx, esophagus:

- Initially, the inlet of the larynx begins as a slit-like opening, known as the laryngeal orifice. It is what maintains the communication between the pharynx and the RT.



- The esophagus descends into the abdomen during development due to the growth of surrounding structures like the pericardium, heart, and lungs.

Anomalies of the trachea and esophagus



The most common developmental abnormalities involving the connection between the respiratory and GI tracts are tracheoesophageal fistulas (TEF) and esophageal atresia.

1. Most Common Anomaly:

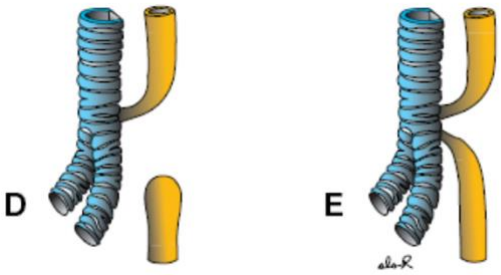
Proximal esophageal atresia with a distal tracheoesophageal fistula.

- Occurs in 90% of cases and affects approximately 1 in 3,000 births.
- Proximal esophageal atresia is also known as the blind end of the esophagus.

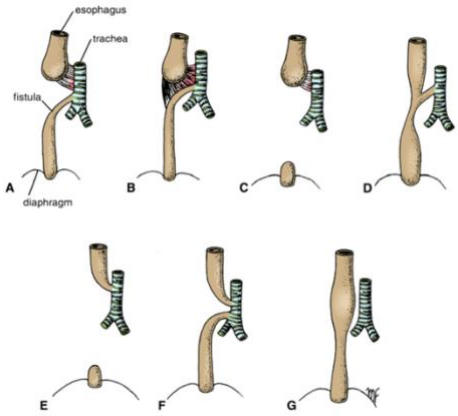
2. Other, Less Common Types:

H-shaped fistula. (E)

Distal esophageal atresia with a proximal tracheoesophageal fistula. (D)



(Pic on the right shows other common cases)



The Complications of TEF

1. Polyhydramnios:

This is the opposite of oligohydramnios (reduced amniotic fluid).

It occurs when atresia prevents amniotic fluid from being absorbed by the fetus. As a result, amniotic fluid builds up in the amniotic sac, leading to an increase in amniotic fluid volume.

2. Pneumonitis:

In cases of a fistula, fluids can move from the gastrointestinal tract to the respiratory tract, causing inflammation of the lungs.

3. Abdominal Bulge:

Air can move from the respiratory tract into the GI tract through the fistula, causing a bulging abdomen each time the baby cries.

4. Other anomalies:
   - Cardiac anomalies (33%).(especially with esophageal atresia)
   - Vertebral anomalies.
   - Anal anomalies.
   - Renal anomalies.
   - Limb defects.

*Tracheal Atresia and Stenosis: **rare** conditions that lead to partial airway obstruction.

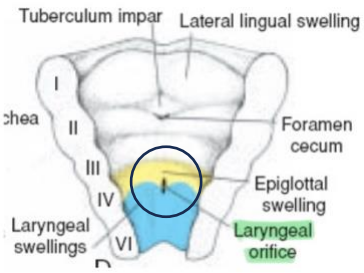
Development of the Larynx

Embryological Origin:

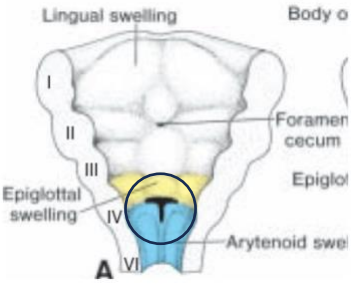
- The cartilage (thyroid, cricoid, arytenoid) and muscles of the larynx originate from the mesodermal mesenchyme of the 4th and 6th pharyngeal arches.
- Lining Epithelium: endoderm.

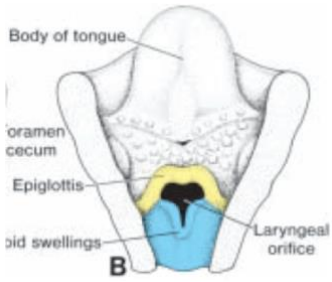
Stages of Development

1. Initial development



Laryngeal inlet changes from a slit-like opening to a T-shaped opening





When larynx cartilages (thyroid, cricoid, arytenoid) develop, a permanent laryngeal opening forms. The epiglottis also forms alongside the cartilages.

2. **Proliferation** of cells

Cells from the endoderm and mesenchyme proliferate rapidly inside the larynx. This proliferation causes a temporary **occlusion** of the laryngeal lumen (filled with cells).

3. **Canalization** and Vacuolization:

- They occur on the lateral walls of the larynx to reopen the lumen.

These stages (2+3) are necessary for forming the following structures:

- Ventricles and saccule on the lateral wall.
- True vocal cords (below the ventricle).
- False vocal cords (above the ventricle).

Nerve Supply of the Larynx

The vagus nerve provides the main innervation, with specific branches innervating different parts:

- External branch of the superior laryngeal nerve: Supplies the cricothyroid muscle (from the 4th pharyngeal arch).
- Recurrent laryngeal nerve: Supplies the rest of the laryngeal muscles (from the 6th pharyngeal arch).

Laryngeal Anomalies

1. Laryngeal Atresia:

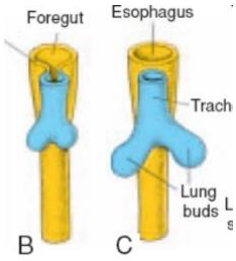
A rare condition also known as Congenital High Airway Obstruction Syndrome (CHAOS). It leads to obstruction of the upper airway passage, resulting in:

- Enlargement of the lungs (air is trapped to compensate for the obstruction).
- Flattened or upwardly inverted diaphragm
- Ascites (accumulation of serous fluid).

*Diagnosis is typically done using ultrasonography.

Development of the Trachea, Bronchi, and Lungs

(They all develop from the lung buds.)



- During its separation from the foregut, the lung bud forms the trachea and two lateral outpocketings, the bronchial buds. At the beginning of the fifth week, each of these buds enlarges to form right and left bronchi.

  (A in pic below)
- As development continues, each main bronchus attains its shape:
  - Right main bronchus: More vertical, wider, and shorter.
  - Left main bronchus: More horizontal, narrower, and longer.

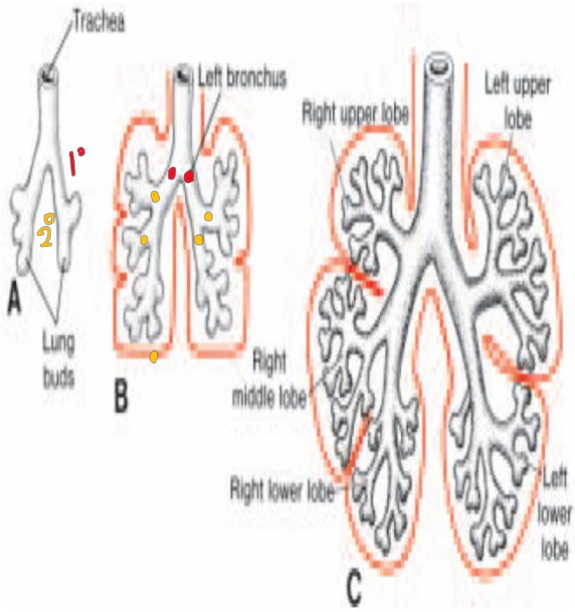
- Formation of Secondary and Tertiary Bronchi:

The secondary bronchi form from the main bronchi and enter the lobes of the lungs:

- Right lung: Three secondary bronchi (one for each lobe).
- Left lung: Two secondary bronchi (one for each lobe).

The tertiary bronchi (bronchopulmonary segments) develop next (B):

- Right lung: Ten bronchopulmonary segments:



Right upper lobe: apical, anterior, posterior

Right middle lobe: medial, lateral

Right lower lobe: Five basal segments

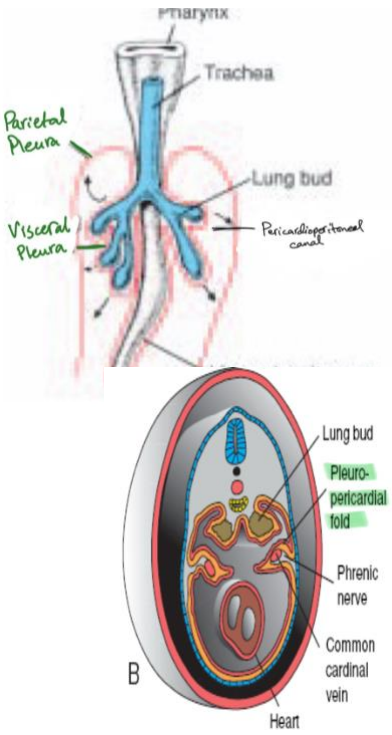
- Left lung: Eight bronchopulmonary segments:

Left upper lobe: Apicoposterior, anterior, superior and internal lingual

Left lower lobe: Superior, anteromedial, lateral, posterior.

*apicoposterior -> apical & posterior, anteromedial -> anterior & medial.

➢ Development of Pleura and Lung Space



The spaces for the lungs, the pericardioperitoneal canals, is where the lung and bronchi grow. It divides into two parts:

- Pericardial: Surrounds the heart.
- Peritoneal: Surrounds the abdominal cavity.

The pleuropericardial fold is upwards, giving a space for the pleura. (The lungs grow and develop in the pleuropericarial spaces).

The mesoderm, which covers the outside of the lung, develops into the visceral pleura. (The pleura adherent to bronchi)

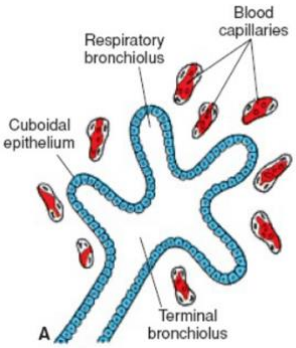
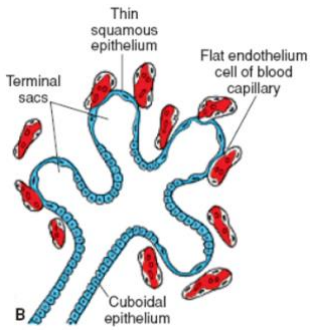
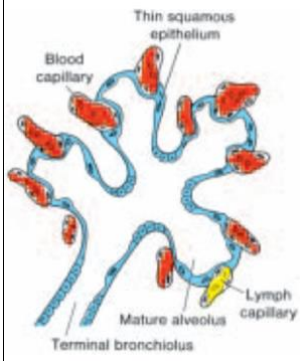
The somatic mesoderm layer, covering the body wall from the inside, becomes the parietal pleura.

The space between the parietal and visceral pleura is called the pleural cavity.

➢ Dichotomous Division and lung positioning

- The bronchopulmonary segments undergo dichotomous division 17 times during fetal development, resulting in 17 generations of branching. (Division after segment)
- Postnatally, the lungs undergo six additional divisions, leading to a total of 23 generations of bronchi.
- These divisions give rise to the alveolar sacs and alveoli
- The divisions are driven by the activity of fibroblast growth factor (FGF).
- 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 thee fourth thoracic vertebra.

- Maturation of the lungs (4 phases)

Pseudoangular period	Canalicular period	Terminal sac period	Alveolar period
5-16 weeks	16-26 weeks (about 6 months)	26 weeks to birth	8 months to childhood
Branching has continued to form terminal bronchioles. No respiratory bronchioles or alveoli = (only conducting) = no respiration in this phase	Each terminal bronchiole divides into2 or more respiratory bronchioles, which in turn divide into 3-6 alveolar ducts. (Still no respiratory membranes) =no gas exchange, no respiration	Terminal sacs (primitive alveoli) form, and capillaries establish close contact. =respiratory membrane betweeen capillaries has developed= There's respiration . That's why a baby born after 7 months can live!	Mature alveoli have well-developed epithelial endothelial (capillary) contacts. =well-developed respiratory membranes
			
	Still terminal bronchioles, resp bronchioles start to develop. Cell type: cuboidal Capillaries are away from respiratory bronchioles	Terminal sacs or primitive alveoli Cell type: simple squamous (starts transitioning) Capillaries are adherent to alveolar cell to form resp membrane	Mature Alveoli (full maturation after birth) Cell type: all are simple squamous Capillaries are more in contact with alveolar cells (type 1) Lymph capillaries form. Surfactant-producing Cells (type 2 alveolar) also form.

- The production of surfactant increases significantly, especially during the last two weeks before birth.
- During birth, a newborn's respiratory tract is filled with fluid that must be cleared to allow normal breathing. This fluid originates from secretions from different cells, glands and surfactant. Stimulating the newborn to cry (e.g., by tapping the baby's back) helps the lungs expand and forces remaining fluid into the interstitial spaces for absorption.
- The most critical factor in breathing is the formation of the surfactant membrane, which lines the alveolar walls (the lining of type I alveolar cells). Surfactant reduces surface tension, allowing the alveoli to expand properly. In the absence of surfactant, **respiratory distress syndrome** occurs, also called hyalie membrane disease. (atelectasis during expiration)
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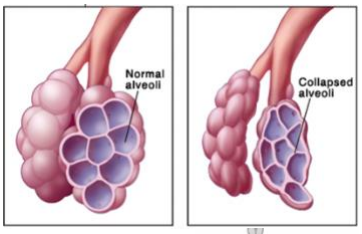
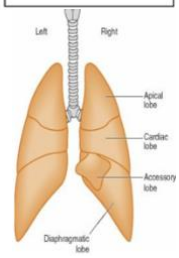
Anomalies of the Respiratory Tract:



- **RDS** (Respiratory Distress Syndrome) in premature infants occurs due to the collapse of the lungs during expiration, resulting from a loss of surfactant. However, today, surfactant can be administered artificially, or medications such as thyroxine and cortisone (betamethasone) can be used to stimulate surfactant production. RDS accounts for 20% of neonatal deaths.

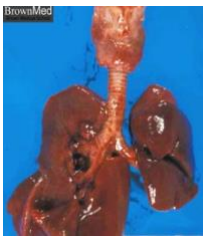


- **Ectopic Lung**: This occurs when there are additional lung buds, resulting in an abnormal number of lobes, such as four lobes in the left lung instead of the usual two.

- **Oligohydramnios**: A condition characterized by decreased amniotic fluid, which is crucial for the maturation of the respiratory tract organs. Insufficient amniotic fluid can lead to pulmonary hypoplasia.

- **Congenital Lung Cysts**: These can be either single or multiple. The most significant complication of these cysts is chronic lung infections.

- **Lung Hypoplasia**: This condition involves the shrinkage or reduction in lung size, often associated with congenital diaphragmatic hernia, which typically occurs on the left side. When an organ is pushed upwards, it exerts pressure on the left lung, leading to decreased lung size, which can cause asphyxia.



Lung Testing in Newborns:

- In the case of stillbirth, when lung tissue is placed in water, it will sink.
- However, if the baby was born alive but later died, the lung tissue will float when placed in water.

This simple test can differentiate between these two cases. If the lung tissue from a live-born infant floats, it may indicate a medical error, and the doctor could be held responsible.

Weeks of development: a summary

- Facial prominences: Fourth week
- Nasal pits from nasal placode: Fifth week
- Fusion between medial nasal and maxillary prominences: Sixth-seventh week
- Fusion of lateral shelves of secondary palate: Seventh week
- Fusion of the two folds of the soft palate: Eighth week
- Fusion of the two parts of the uvula: 11th week
- Beginning of development of the respiratory system: Fourth week
- Respiratory bud, lung bud, respiratory diverticulum appearance: Fourth week

Development of the lung:

- Pseudoglandular period: Fifth to 16th weeks
- Canalicular period: 16th to 26th weeks
- Terminal sac period: 26th weeks to birth
- Alveolar period: 8 months to childhood

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2	16	Sinks	Floats
V2→V3			