
بسم الله الرحمن الرحيم

DOPAMINE SCIENTIFIC TEAM

**EMBRYOLOGY**

**MID | Lecture 1**

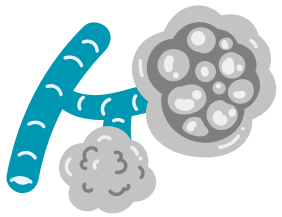
# Development of the Respiratory Tract

**Written by:** Bisher Khashashneh
Omar Ibrahim

**Reviewed by:** Omar Ibrahim

﴿ 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:** القوي الغالب الجليل رفيع الشأن، قهر جميع المخلوقات، ودانت له وخضعت لقوته.

**الورود:** ورد في القرآن (٩٢) مرة.

**الشاهد:** ﴿وَٱعْلَمْ أَنَّ ٱللَّهَ عَزِيزٌ حَكِيمٌ﴾ [ البقرة:٢٦٠ ].

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*اضغط هنا لشرحٍ أكثر تفصيلًا*

# Respiratory System Embryology

*الباقيات الصالحات: سبحان الله والحمد لله ولا إله إلّا الله والله أكبر*

**Doctor's advice:**

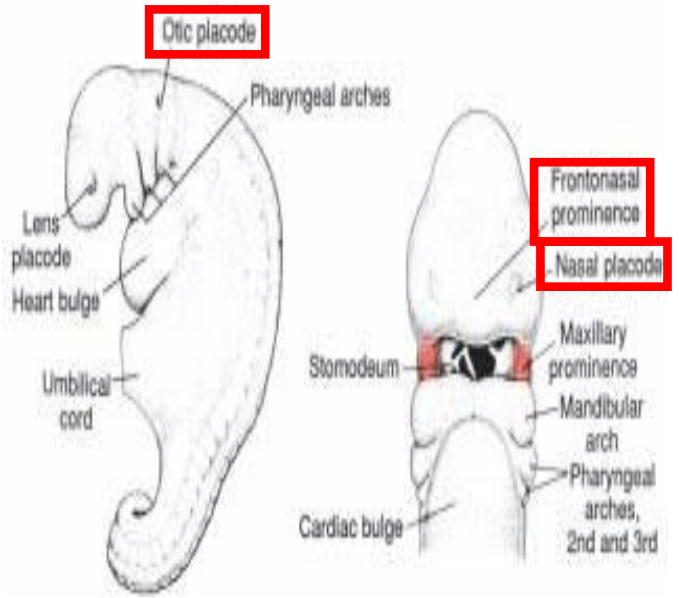
When studying embryology, always try to visualize the final anatomical structure of the organ. Understanding the adult anatomy makes the developmental steps easier to follow and remember.

For example, the nose consists of two nasal cavities separated by a septum, each having medial and lateral walls, three nasal conchae, and anterior and posterior openings. By keeping this final anatomical arrangement in mind, embryological changes can be understood as steps that progressively shape the mature structure.

# Development of the Nose and Upper Lip

## ➢ Ectodermal Placodes: Sites of Sensory Organ Development

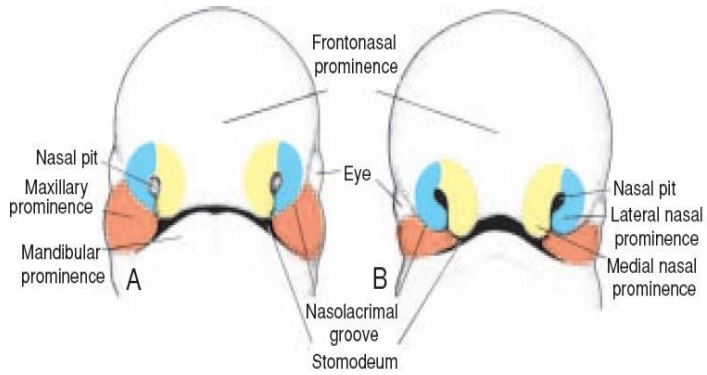
- The **otic placode** (*"otic" = ear*) is a localized thickening of the **surface ectoderm** and represents the site where the **auditory (inner ear) structures** begin to develop.
- Similarly, the **nasal placode**, also called the **olfactory placode**, is a thickening of the **surface ectoderm** that invaginates into the nasal cavity to form the **nasal pit, which initially forms the nostrils (nares),** and then continued invagination of the nasal pit also forms of the **vestibules**.




*Doctor's Figure*

## ➢ Facial Prominences: Mesenchymal Centers of Growth

- In contrast to placodes, **facial prominences** are **mesenchymal in origin** and serve as the **main growth centers** responsible for shaping the skeletal structure of the face.
- One of the earliest and most important facial prominences is the **frontonasal prominence**, which develops in the region of the **frontal bone**.
- The frontonasal prominence extends downwards and gives rise to:
  1. The **nasal septum** (Superior Part)
  2. The **medial nasal prominences**
  3. The **lateral nasal prominences**



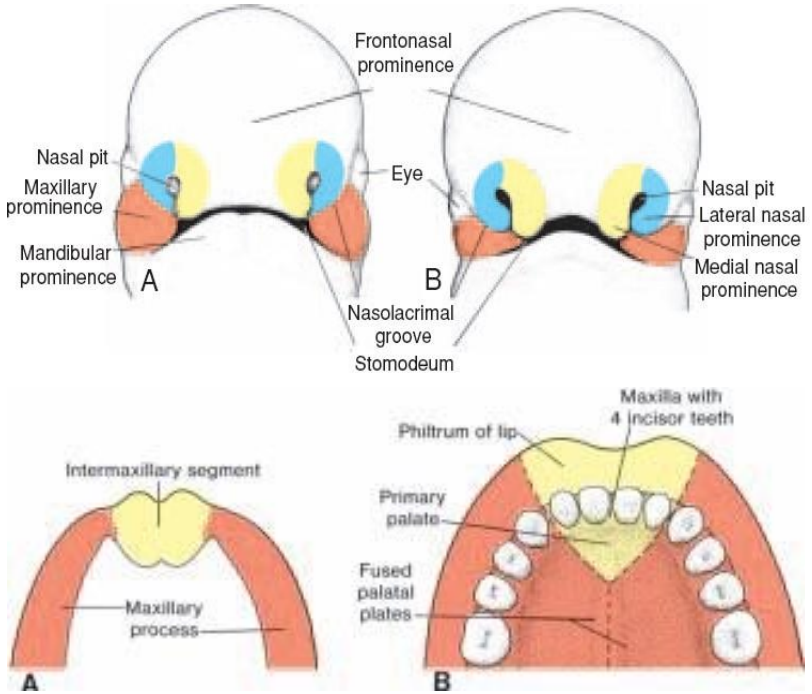

*Doctor's Figure*

# Development of the Nose and Upper Lip

- **Lateral Nasal Prominences** (blue areas) form:
  - The **alae of the nose**
  - The **lateral wall of the nasal cavity**

- **Medial Nasal Prominences** (yellow areas) grow **toward the midline** and fuse with each other forming:
  - The **tip and crest of the nose**
  - The **inferior (end) part of the nasal septum**
  - The **Inter-Maxillary Segment,** which forms:
    - ✓ The **philtrum** of the upper lip
    - ✓ The **medial one-third of the upper lip**
    - ✓ The **primary palate**
    - ✓ The **alveolar part of the maxilla that contains the upper four incisor teeth**

- **Maxillary Prominences** (red areas) start to fuse with the **medial nasal prominences** at the **fifth week** to form the **lateral two-thirds of the upper lip.**
- **This fusion process** takes **2 weeks** to complete.
- **Failure of fusion** between a maxillary prominence and the medial nasal prominence results in a **cleft lip** that could be either **unilateral or bilateral**




*Doctor's Figures*

So the **Nasal Septum** is divided developmentally to two parts:

1. **Superior Part → Frontonasal Prominence**
2. **Inferior Part → Medial Nasal Prominences**

# Development of the Nose and Upper Lip Summary

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 |

[a] The frontonasal prominence is a single unpaired structure; the other prominences are paired.

*Doctor's Figure*

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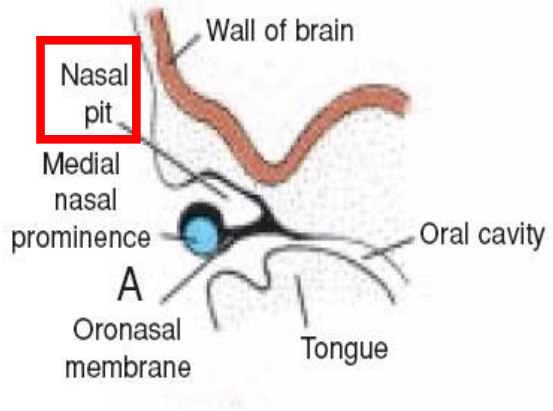
# Development of the Nasal Cavities

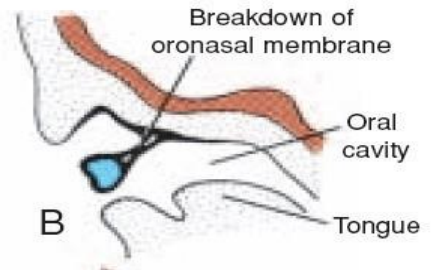
➢ **Division of the Developing Nasal Cavity:**

- The developing nasal cavity can be understood as having **two parts**:
  - ✓ An **anterior –initial- part (Nares and the Vestibule)**
  - ✓ A **posterior –deep- part (The Definitive Nasal Cavity)**




➢ **Anterior (Initial) part,** formed by the **nasal pits (Invagination of the nasal placodes):**

- These pits give rise to the **external nares (nostrils)** and the **nasal vestibule**.
- This region is **already open to the exterior** early in development due to **invagination of the surface ectoderm**.

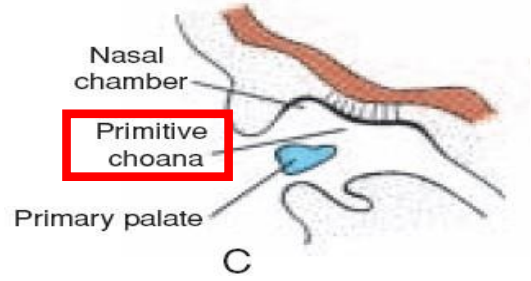



➢ **Posterior (Deep) part,** formed by the **medial and lateral nasal prominences:**

- In this region, **mesenchymal cells proliferate**, temporarily filling the developing cavity.
- This is followed by **vacuolization and canalization**, which recreate the lumen and form the **definitive nasal cavities**.

➢ **Relationship to the Oral Cavity and Palate:**

- Initially, the posterior nasal cavities are separated from the oral cavity by the **oronasal membrane**.
- This membrane later **ruptures**, creating a temporary communication with the oral cavity called the **Primitive Choana**.
- With **formation of the primary and secondary palates at the site of the ruptured oronasal membrane**, the position of the choanae shifts **posteriorly**, this results in the **definitive choanae**, which open into the **nasopharynx.**




**Sagital Sections**

*Doctor's Figures*

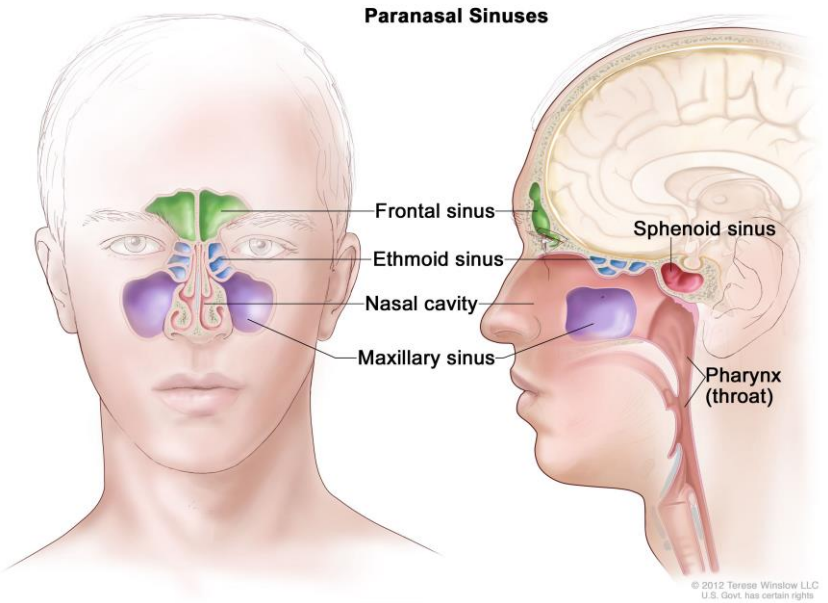
# Development of the Paranasal Sinuses

- All paranasal sinuses develop as **outgrowths from the lateral wall of the nasal cavity**.

- **Initial Formation**
  - Development begins at the **sites where the sinuses open into the nasal cavity**.
  - At these openings, **epithelial proliferation** occurs from the **lateral nasal wall**, forming a **sinus duct**.

- **Cavity Formation**
  - As the proliferating epithelium extends into the adjacent bone (e.g., the maxilla for the maxillary sinus), it undergoes **canalization**.
  - This process creates a **mucosa-lined cavity within the bone**, which represents the developing sinus.

- **Growth and Maturation**
  - Initially, the sinus cavity is **small and rudimentary**.
  - With continued **growth of the facial bones**, the sinus **progressively enlarges** until it reaches its **adult size**.



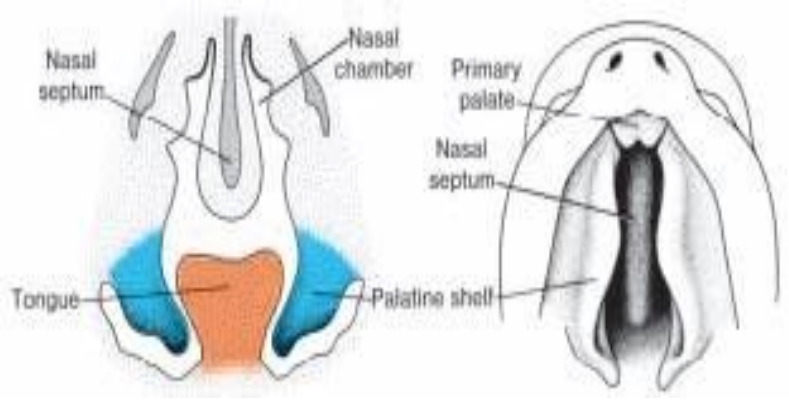

**Example: Maxillary Sinus**
- The **maxillary sinus** opens into the **middle meatus** through the **hiatus semilunaris**.
- Proliferation begins at this opening, forming the **maxillary sinus duct**, which then extends into the maxilla and start forming the sinus cavity within the maxilla by canalization.

# Primary and Secondary Palates

➢ **Primary Palate**

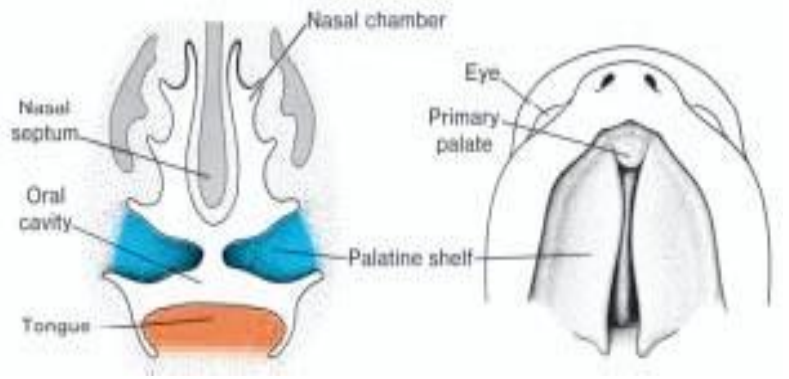
•The **primary palate** is formed from the **intermaxillary segment**, which results from the fusion of the **medial nasal prominences**.

•It is continuous with the **inferior part of the nasal septum** -which is also derived from the medial nasal prominences- together they contribute to the **initial division of the nasal cavity**.




➢ **Secondary Palate**

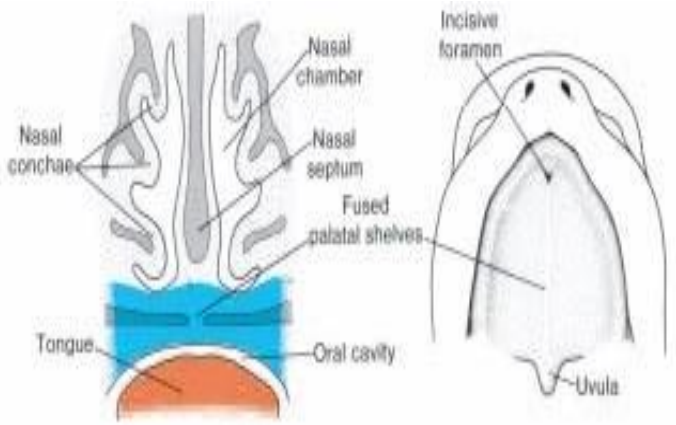
- The **secondary palate** starts to develop during the **sixth week** from paired **palatine shelves**, which are **outgrowths of the palatine bones** **(however multiple anatomy references indicate that the palatine shelves are outgrowths of the maxillary prominences)**
- These palatine shelves grow medially above the tongue, and **fuse in the midline** at the **seventh week**, forming the **secondary palate**.
- Following fusion, the secondary palate undergoes **ossification**, resulting in the **hard palate**:
  - ✓ **Anterior part** → ossifies → **hard palate** (**palatine processes of the maxilla + horizontal plates of the palatine bones)**
  - ✓ **Posterior part** → remains non-ossified → **soft palate and uvula**
- Formation of the secondary palate **completely separates the oral and nasal cavities** and displaces the **primitive choanae posteriorly**, creating the **definitive (adult) choanae**.




*Doctor's Figures*

# Development of the Incisive Foramen

- During fusion of the **primary and secondary palates**, a small opening remains at their junction, forming the **incisive foramen**. This foramen represents the boundary between the primary and secondary palates, allowing the passage of the **greater palatine nerve and vessels** from the oral cavity to the nasal cavity.




*Doctor's Figures*

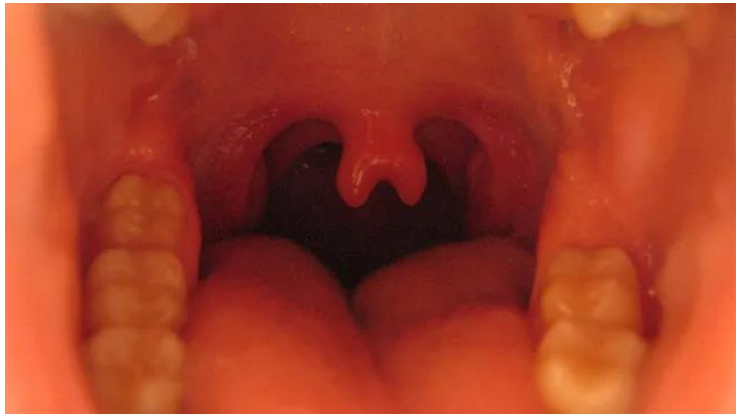
# Development of the Soft Palate and Uvula

➢ **Origin:**

- The **palatine shelves** fuse in the midline to form the **secondary palate**.
- **Posteriorly**, these shelves extend backward.
- The **posterior extensions do not undergo ossification**, giving rise to the **soft palate and uvula**.


➢ **Paired Development:**

- Both the **soft palate and the uvula** develop from **paired palatine shelves**, one from each side.
- Normal development requires **midline fusion** of these paired structures.
- In some individuals, the uvula appears **split at the midline (bifid uvula)**, reflecting **incomplete fusion** of its two embryonic components.



Bifid Uvula

➢ **Timeline:**

- **Soft palate:** forms around the **8th week** of embryonic development.
- **Uvula:** forms later, around the **11th week** of embryonic development.

# Development of the Respiratory System

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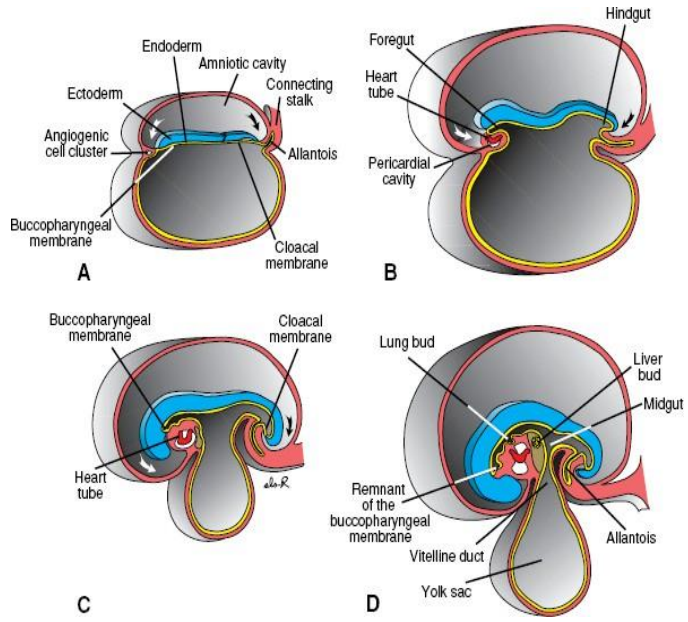
# Remember: Development of the Respiratory System

- During fetal life, the **endodermal gut tube** extends from the **buccopharyngeal (oropharyngeal) membrane** to the **cloacal membrane** and is divided into **four segments**:
  - ✓ **Pharyngeal gut:** extends from the buccopharyngeal membrane **to the level at which the respiratory diverticulum begins.**
  - ✓ **Foregut:** extends **just distal to the pharyngeal gut** to the **upper half of the duodenum**; supplied by the **celiac trunk**.
    → Gives rise to the **respiratory diverticulum**.
  - ✓ **Midgut:** extends from the **lower half of the duodenum** to the **proximal two-thirds of the transverse colon**; supplied by the **superior mesenteric artery**.
  - ✓ **Hindgut:** extends from the **distal one-third of the transverse colon** to the **upper half of the anal canal**; supplied by the **inferior mesenteric artery**.

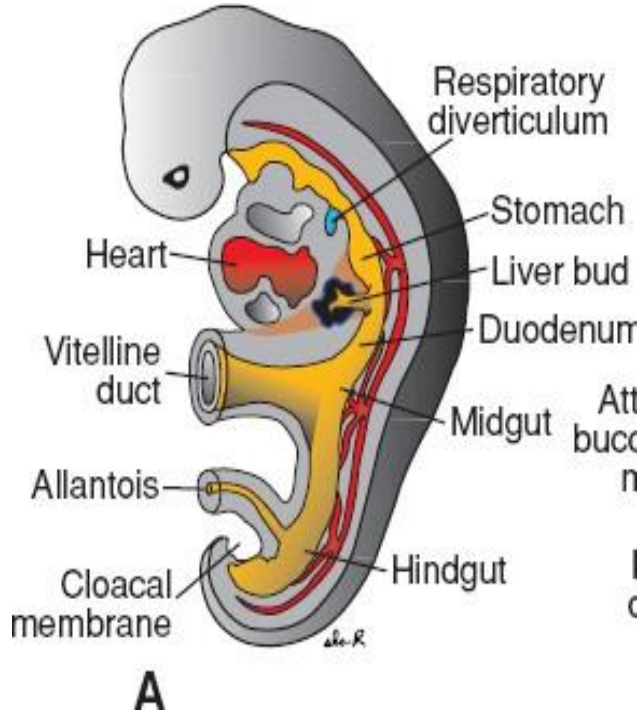



*Doctor's Figure*

- The **hepatic (liver) diverticulum** arises from the **junction between the foregut and midgut**, at the midpoint of the duodenum.

# Development of the Respiratory System

- At **Week 4:** Respiratory development begins when **fibroblast growth factors (FGFs)** stimulate the **ventral wall of the foregut** (The upper portion of it, just caudal to the pharyngeal gut)
- This stimulation induces formation of the **respiratory bud**, which expands then to form the **respiratory diverticulum**.
- The diverticulum proliferates and differentiates forming the **trachea**, **primary bronchi**, **secondary (lobar) bronchi**, and **tertiary (segmental) bronchi** sequentially.
- Continued branching and differentiation give rise eventually to the **bronchioles** and ultimately the **alveoli**.

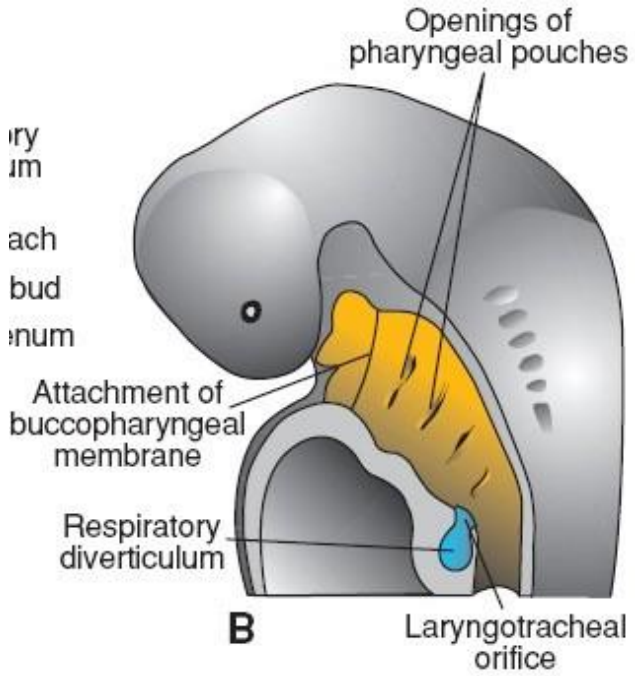



*Doctor's Figure*

# Development of the Respiratory System

- The **epithelium** of the internal lining of the larynx, trachea, and bronchi, as well as that of the lungs, is entirely of **endodermal origin.**

- The **cartilaginous, muscular,** and **connective tissue** components of the trachea and lungs are derived from **splanchnic mesoderm** surrounding the foregut.

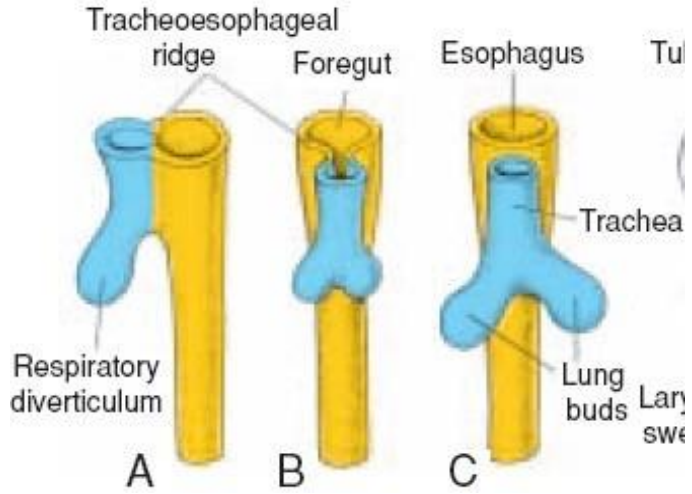



*Doctor's Figure*

# Separation of the Respiratory Tract from the Foregut

- **Initial Formation:**
  The respiratory tract initially develops as a **ventral outpouching of the foregut,** at this stage, the **respiratory diverticulum and foregut are still continuous**.

- **Formation of Tracheoesophageal Ridges:**
  During the **fifth week**, continued growth of the respiratory diverticulum leads to the appearance of **paired longitudinal ridges** on the lateral walls of the foregut **just posterior to the diverticulum,** known as the **tracheoesophageal ridges**.



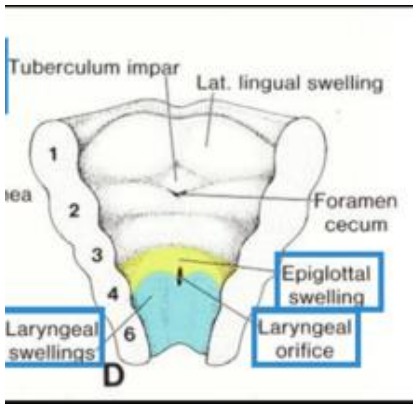

*Doctor's Figure*

- **Development of the Tracheoesophageal Septum:**
  The tracheoesophageal ridges proliferate and **fuse in the midline**, forming the **tracheoesophageal septum**.

- **Final Separation:**
  Fusion of the septum divides the primitive foregut into:
  - ✓ An **anterior respiratory tube** (trachea and lung primordium)
  - ✓ A **posterior esophagus**

# Development of the Laryngeal Orifice

- Following separation of the respiratory diverticulum from the foregut, the **laryngeal orifice remains as the only persistent embryonic communication between the pharynx and the developing respiratory tract**, connecting the foregut-derived pharynx to the larynx.
- This opening later remodels to form the **adult laryngeal inlet**.
- The **laryngeal orifice** initially appears as a **slit-like opening** between the **epiglottic swelling** anteriorly and the **laryngeal swelling** posteriorly.
- With enlargement and medial growth of the laryngeal swelling, the orifice becomes **temporarily T-shaped**.
- As development continues and the **epiglottis forms**, the laryngeal orifice remodels and **eventually forms the adult-shaped laryngeal inlet**.

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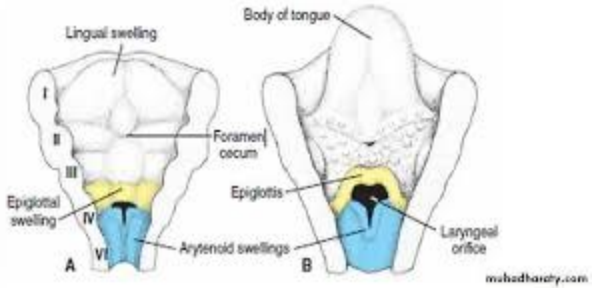


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# Development of the Esophagus

## ➢ Lengthening:

Initially, the **esophagus is short, it elongates progressively** as a result of:

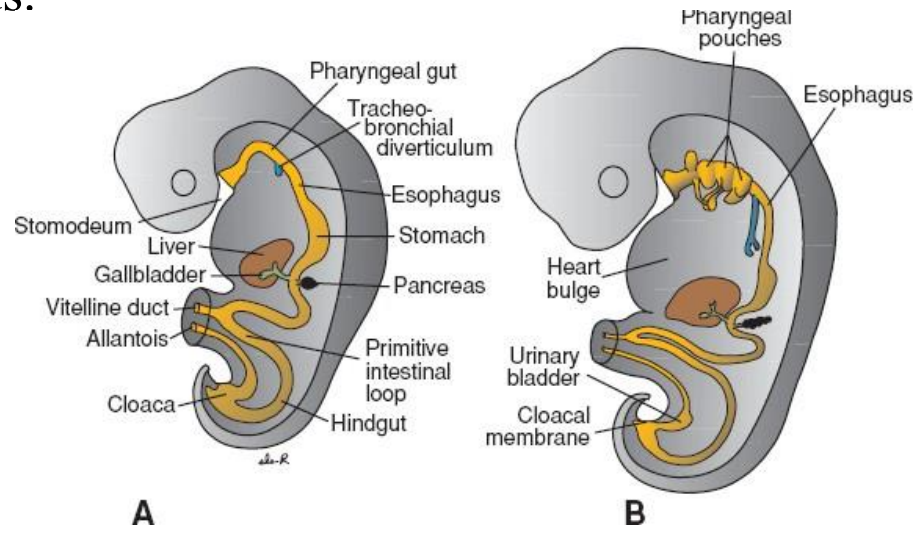
- **Descent of the heart**
- **Growth and caudal displacement of the lungs**

This elongation establishes the final position and length of the esophagus.

## ➢ Muscular Development:

The esophageal wall differentiates into two muscle types:

- **Upper one-third: Striated (skeletal) muscle**
- **Lower two-thirds: Smooth muscle**




*Doctor's Figure*

## ➢ Innervation:

- **Upper (striated) part:**
  Innervated by **motor fibers from the vagus nerve (CN X)**
- **Lower (smooth muscle) part:**
  Innervated by the **autonomic nerves from the splanchnic plexus.**

# Anomalies of the Trachea and Esophagus

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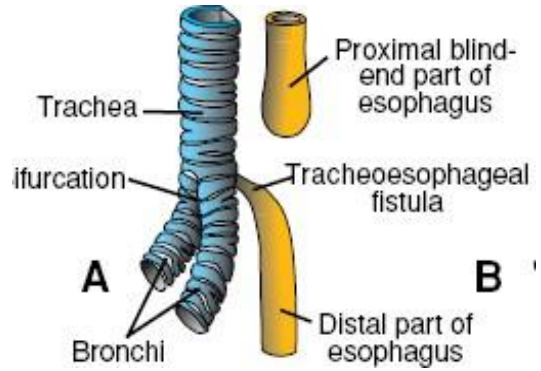
# Esophageal Atresia and Tracheoesophageal Fistula

- The **most common congenital anomalies of the esophagus** are **esophageal atresia and tracheoesophageal fistulas (TEF)**.

- **Embryological Cause:**

These anomalies result from **abnormal separation of the foregut into the trachea and esophagus**

The underlying defect is **abnormal development or fusion of the tracheoesophageal ridges**, leading to incomplete or incorrect formation of the **tracheoesophageal septum**.

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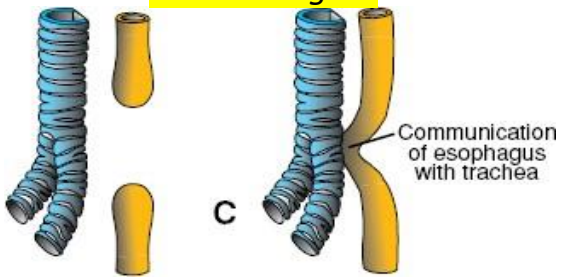
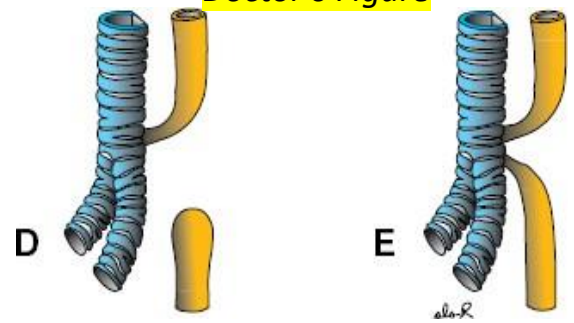



*Doctor's Figure*

- **Types:**

Esophageal atresia and TEF can occur in several configurations, including: **Pure esophageal atresia (double atresia), isolated tracheoesophageal fistula (H-type), proximal fistula, distal fistula with esophageal atresia and proximal esophageal atresia with distal tracheoesophageal fistula**




*Doctor's Figure*

- **The Most Common Type:**

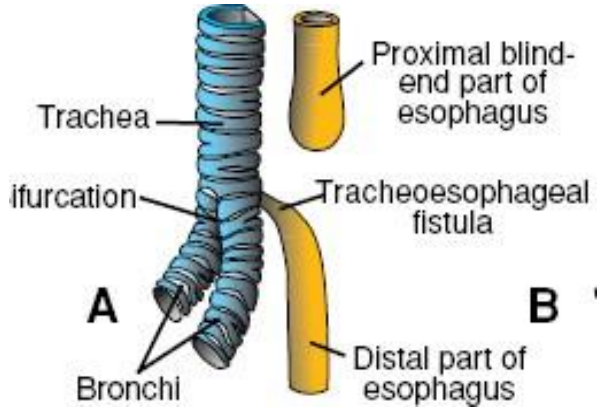
**Proximal esophageal atresia with distal tracheoesophageal fistula**

Occurs in approximately **1 in 3,000 live births**.

# Complications of Proximal Esophageal Atresia with Distal Tracheoesophageal Fistula

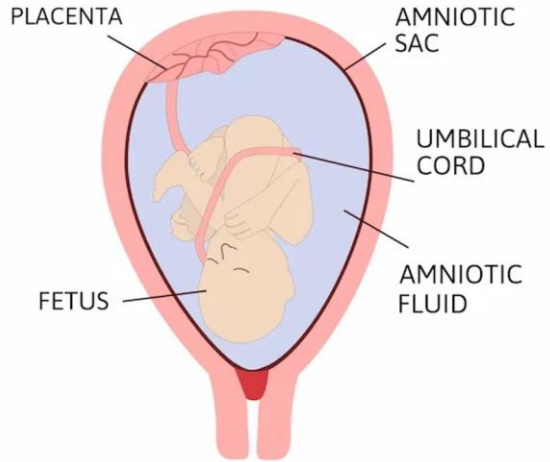
## ➢ During Fetal Life:

- The primary complication is **polyhydramnios**.
- Normally, the fetus **swallows amniotic fluid**, which is absorbed through the gastrointestinal tract and partially excreted as urine back into the amniotic cavity.
- In the presence of **esophageal atresia**, swallowed amniotic fluid **cannot reach the stomach**, leading to **regurgitation into the amniotic cavity**.
- As a result, normal absorption of amniotic fluid is impaired, causing **excess accumulation of amniotic fluid (polyhydramnios)**.




## ➢ After Birth:

- **Feeding difficulties:**
  The infant regurgitates milk shortly after feeding due to the blind-ending proximal esophagus.
- **Respiratory complications:**
  The **distal tracheoesophageal fistula** allows **gastric contents and acid** to enter the trachea, causing **chronic respiratory infections and pneumonia**.
- **Abdominal distension:**
  Air passes from the trachea into the stomach through the fistula, especially during crying, causing **progressive gastric distension and abdominal enlargement**.



POLYHYDRAMNIOS

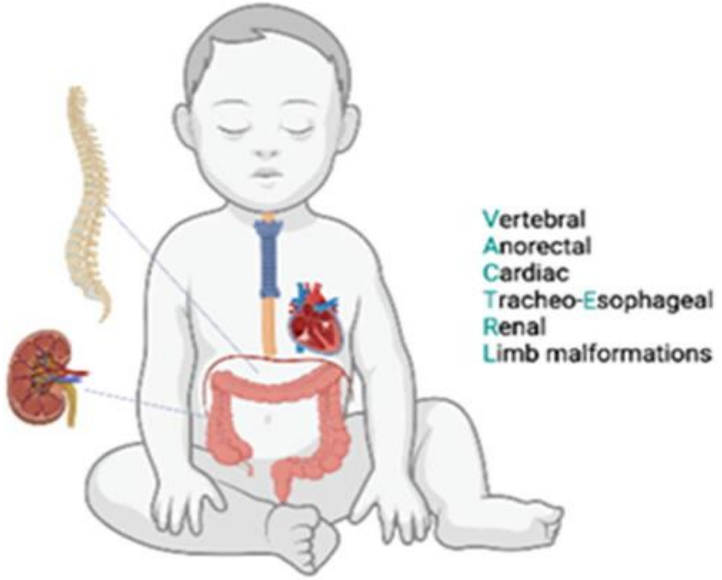
➢ **Surgical correction** is immediately indicated after birth.

# Associated Anomalies in Esophageal Atresia

- Esophageal atresia is **usually part of a constellation of congenital anomalies** that tend to occur together, collectively known as the **VACTERL association**.

  **VACTERL mnemonic:**

  **V** – Vertebral anomalies
  **A** – Anal atresia
  **C** – Cardiac defects
  **T** – Tracheoesophageal fistula
  **E** – Esophageal atresia
  **R** – Renal anomalies
  **L** – Limb anomalies

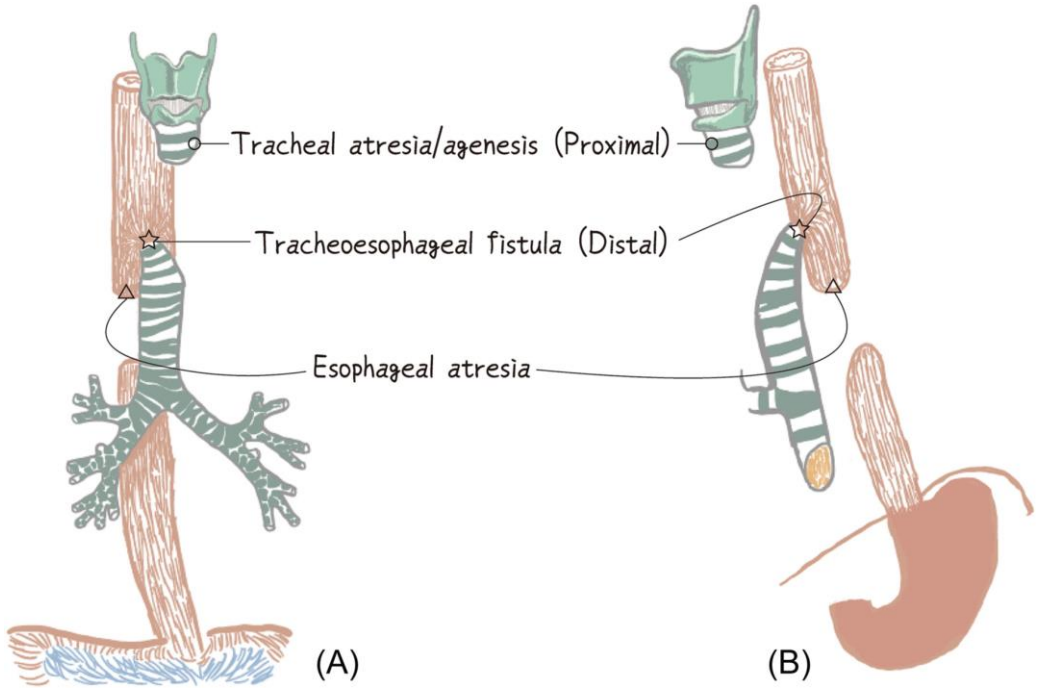



- The most commonly associated anomalies with the esophageal atresia are **cardiac defects (33% association)**, including: Ventricular septal defect (VSD), Atrial septal defect (ASD), Tetralogy of Fallot and other congenital heart defects.

# Tracheal Atresia and Stenosis

- A **rare and uncommon** congenital abnormality characterized by the presence of **web-like tissue** that obstructs airflow through the trachea.

- **Surgical correction is indicated immediately after birth**.

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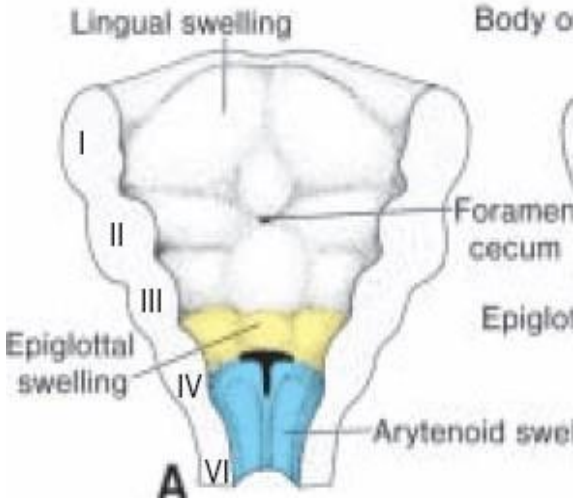
# Development of The Larynx

# Embryological Development of the Larynx

➢ **Tissue Origins:**

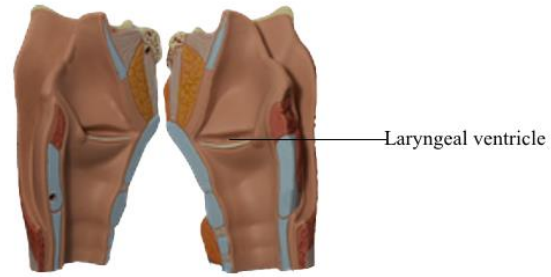
- The **epithelial lining of the larynx** is derived from **endoderm**.
- The **laryngeal cartilages and muscles** arise from **splanchnic mesoderm** of the **4th and 6th pharyngeal arches**.

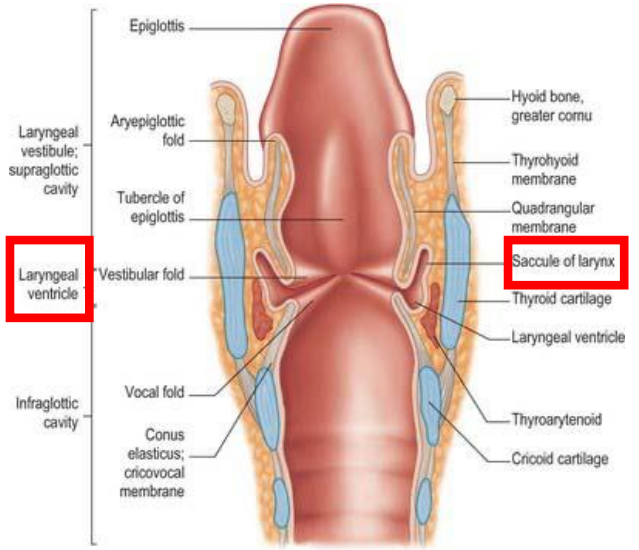



*Doctor's Figure*

# Development of the Laryngeal Lumen

- During early laryngeal development, the **endodermal epithelium proliferates throughout the laryngeal cavity**, this proliferation causes a **temporary occlusion of the whole laryngeal lumen**.
- **Vacuolization and recanalization** then occur within this epithelial plug, however this recanalization doesn't happen in a uniform manner:
  - In the **upper part of the larynx**, above the vestibular (false vocal) folds, recanalization mainly **reopens the lumen** after its temporary closure.
  - However, **below this level**, recanalization occurs **more prominently on the sides than in the center**. This uneven breakdown of the epithelial plug creates **two lateral spaces**, which become the **laryngeal ventricles**. These ventricles separate the surrounding tissue into an **upper vestibular (false vocal) fold** and a **lower vocal (true vocal) fold**.
- The **walls of these ventricles** give rise to important laryngeal structures:
  - The **upper folds** differentiate into the **vestibular (false vocal) folds**
  - The **lower folds** differentiate into the **vocal (true vocal) folds**
  - In addition, **laryngeal saccules** develop as superior extensions from the laryngeal ventricles.

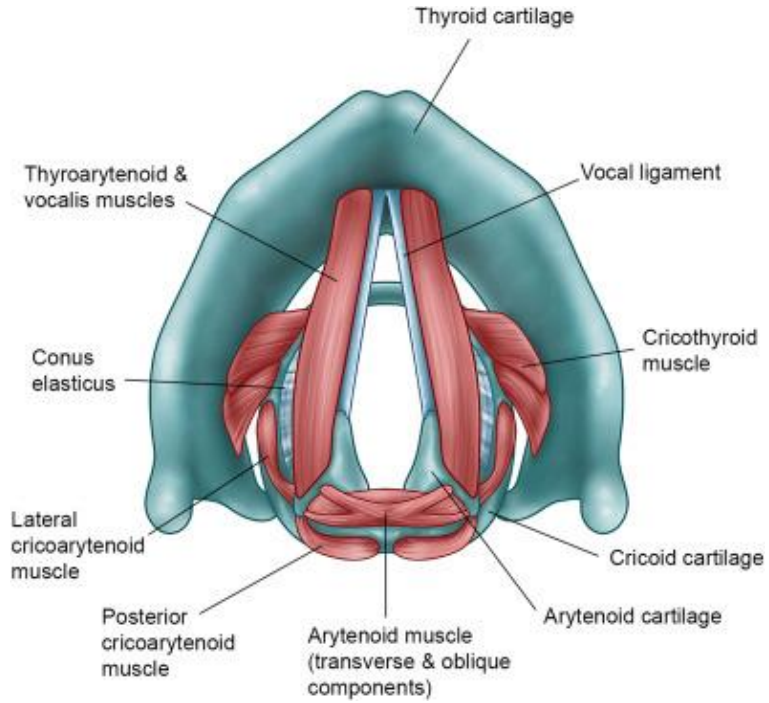



**Proliferation → Occlusion → Recanalization → Ventricles → Folds + Saccules**

# Muscular Development and Innervation

- The **innervation of laryngeal muscles corresponds to their pharyngeal arch of origin**, and all are supplied by branches of the **vagus nerve (CN X)**:
- **4th pharyngeal arch muscle**:
  - ✓ **Cricothyroid muscle**
  - ✓ Innervated by the **external laryngeal nerve** (branch of the **superior laryngeal nerve**)
- **6th pharyngeal arch muscles**:
  - ✓ All remaining **intrinsic laryngeal muscles**
  - ✓ Innervated by the **recurrent laryngeal nerve**



# Anomalies of the larynx

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# Laryngeal Atresia

- **Laryngeal atresia** is a **very rare congenital anomaly**, similar in severity to **tracheal atresia**, and results in **obstruction of the upper fetal airway**.
- This condition is part of a spectrum known as **Congenital High Airway Obstruction Syndrome (CHAOS), meaning that any other anomaly causing obstruction of the upper part of the airway would cause similar manifestations.**

- **Pathophysiological Changes include:**

1. **Distal to the atresia or stenosis**, the **lungs become enlarged** because:

- Fetal lungs normally produce fluid during development → This fluid cannot escape through the obstructed airway → It accumulates, causing lung overdistension
- As a result, the lungs appear **echogenic** on ultrasound (meaning they reflect more sound waves and look brighter).

2. The **diaphragm becomes flattened** because:

- The enlarged lungs push downward → Normal dome-shaped curvature is lost

3. Increased intrathoracic pressure leads to:

- **Compression of venous return** → Fluid accumulation in the abdomen (**ascites**) and generalized fetal edema (**hydrops fetalis**)

- **Diagnosis:**

**Prenatal diagnosis** is typically made using **ultrasonography**, based on the characteristic findings:

Enlarged, echogenic lungs

Flattened diaphragm

Ascites and signs of hydrops

# Lungs and Bronchial Tree Development

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# Development of the Lungs and Bronchial Tree

➢ **Initial Development**

- Lung development begins with formation of the **trachea** from the respiratory diverticulum.
- At approximately the level of **T4**, the distal end of the trachea divides into the **right and left primary (main) bronchi**.

➢ **Primary Bronchi**

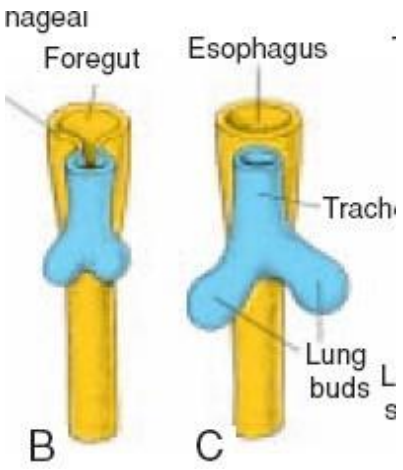
- The **primary bronchi** represent the first branching of the bronchial tree, each primary bronchus enters its respective lung.

➢ **Secondary (Lobar) Bronchi**

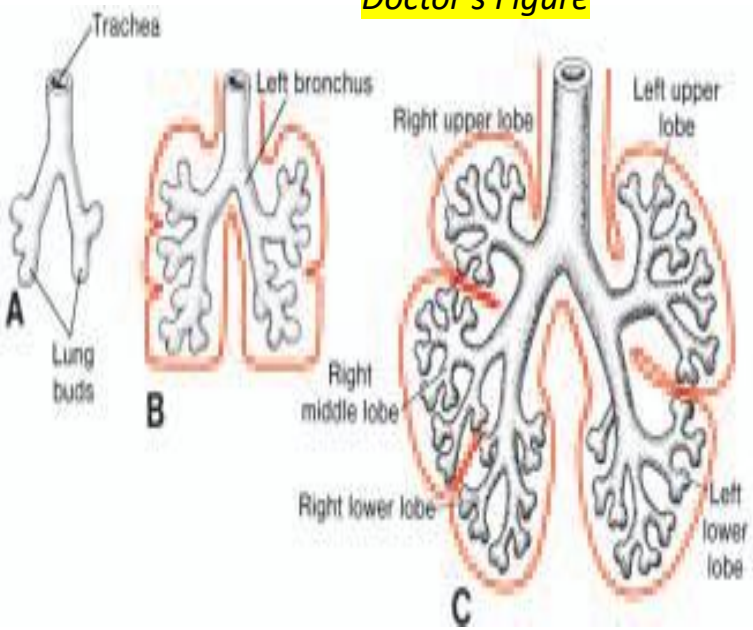
- The primary bronchi then divide into **secondary (lobar) bronchi**, which are **intrapulmonary**.
- These correspond to the **lobes of the lungs**:

  **Right lung,** 3 secondary bronchi:
  - ✓ Superior
  - ✓ Middle
  - ✓ Inferior

  **Left lung,** 2 secondary bronchi:
  - ✓ Superior
  - ✓ Inferior




*Doctor's Figure*




*Doctor's Figure*

# Development of Tertiary (Segmental) Bronchi

- Each secondary bronchus further divides into **tertiary (segmental) bronchi,** and each tertiary bronchus supplies a **bronchopulmonary segment** (anatomically and functionally independent unit).

- **Right Lung – 10 Segmental Bronchi**
  1. **Upper lobe:**
  - ✓ Apical
  - ✓ Posterior
  - ✓ Anterior
  2. **Middle lobe:**
  - ✓ Lateral
  - ✓ Medial
  3. **Lower lobe:**
  - ✓ Superior
  - ✓ Medial basal
  - ✓ Anterior basal
  - ✓ Lateral basal
  - ✓ Posterior basal

- **Left Lung – 8–10 Segmental Bronchi**
  1. **Upper lobe:**
  - ✓ Apicoposterior (fusion of apical + posterior)
  - ✓ Anterior
  - ✓ Superior lingular
  - ✓ Inferior lingular
  2. **Lower lobe:**
  - ✓ Superior
  - ✓ Anteromedial basal (fusion of anterior + medial)
  - ✓ Lateral basal
  - ✓ Posterior basal

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## Key Embryological Dates (Summary Table)

| Week | Main Developmental Events |
|---|---|
| **Week 4** | Formation of the **respiratory bud/diverticulum** from the ventral foregut |
| **Week 5** | Start of **fusion of maxillary prominences** with medial nasal prominences; appearance of **tracheoesophageal ridges** |
| **Weeks 5–7** | Completion of **upper lip fusion** |
| **Week 6** | Initiation of **secondary palate** development (palatine shelves) |
| **Week 7** | **Fusion of palatine shelves** → formation of the secondary palate |
| **Week 8** | Formation of the **soft palate** |
| **Week 11** | Formation of the **uvula** |

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# Thank you

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# EMBRYOLOGY QUIZ LECTURE 1

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# Scan the QR code or click it for FEEDBACK

Corrections from previous versions:

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