

Development of the Respiratory System

The **respiratory system** begins to develop during the **fourth week** of gestation from the **foregut endoderm** and surrounding **splanchnic mesoderm**. Until birth, **maternal-placental circulation** provides all fetal oxygen and removes carbon dioxide.

Origin

- Derived from the **primitive foregut**, an endodermal structure formed during **lateral folding** of the embryo.
- The **respiratory diverticulum (lung bud)** forms as a ventral outpouching of the foregut around **week 4**, under the influence of **fibroblast growth factor (FGF)** signaling from surrounding mesenchyme.

Developmental Stages

Formation of Lung Buds

- Arises from **ventral foregut**.
- Initial **open communication** with foregut.
- **Tracheoesophageal ridges** develop and fuse to form the **tracheoesophageal septum**, separating:
 - **Dorsal esophagus**
 - **Ventral trachea and lung buds**

The **epithelium** of the trachea, bronchi, and lungs is of **endodermal origin**, while the **cartilage, smooth muscle, and connective tissue** are derived from **splanchnic mesoderm**.

Partitioning Defects

Improper septum formation may cause:

Esophageal Atresia (EA) and Tracheoesophageal Fistula (TEF)

- Occur in **~1/3,000** births.
- Most common type: **Proximal esophageal atresia + distal TEF** (90%).
- Associated anomalies: **VACTERL** association:
 - **V**ertebral anomalies
 - **A**nal atresia
 - **C**ardiac defects
 - **TE F**
 - **E**sophageal atresia
 - **R**enal anomalies

- **L** imb defects

Polyhydramnios may develop due to impaired swallowing, and **aspiration pneumonia** can occur due to reflux through fistulas.

Larynx Development

- **Epithelium** from **endoderm** .
- **Cartilages and muscles** from **mesenchyme of the 4th and 6th pharyngeal arches** .
- Early on: **Sagittal slit** ? later forms **T-shaped opening** .
- **Thyroid, cricoid, and arytenoid cartilages** form from mesenchyme.
- Lumen is temporarily obliterated by epithelial overgrowth but later reopens via **vacuolization and recanalization** , forming **laryngeal ventricles** , **true** and **false vocal cords** .

Trachea, Bronchi, and Lung Formation

Branching Morphogenesis

- **Week 5** : Bronchial buds ? **primary bronchi** (right and left).
 - Right: **3 secondary bronchi** (3 lobes)
 - Left: **2 secondary bronchi** (2 lobes)
- Further branching ? **10 segmental bronchi** on right, **8 on left** ? form **bronchopulmonary segments** .
- **FGF10 signaling** from mesenchyme controls branching.

? Bronchi develop as **endoderm-mesoderm interactions** , forming a complex 3D airway tree.

Pleural Development

- **Lung buds** grow into **pericardioperitoneal canals** , later forming **pleural cavities** .
- **Visceral pleura** from **splanchnic mesoderm**
- **Parietal pleura** from **somatic mesoderm**
- **Pleural cavity** : space between these layers

Lung Maturation Stages

Period	Weeks	Key Features
Pseudoglandular	5–16 weeks	Branching ? terminal bronchioles; no gas exchange
Canalicular	16–26 weeks	Formation of respiratory bronchioles , alveolar ducts , and vascularization
Terminal Sac	26 weeks–birth	Primitive alveoli (terminal sacs) and capillary proximity

Period	Weeks	Key Features
Alveolar	8 months–childhood	allow gas exchange Development of mature alveoli and surfactant production

By **week 26** , sufficient terminal sacs and **type I pneumocytes** allow **preterm survival** with support.

Surfactant Production

- **Type II pneumocytes** begin surfactant synthesis at ~ **week 24** .
- Significant increase in production occurs in the **last 2 weeks** of gestation.
- **Surfactant** :
 - Rich in **phosphatidylcholine (lecithin)**
 - Reduces **alveolar surface tension**
 - Prevents **alveolar collapse** during exhalation

Fetal Lung Fluid

- Prior to birth, lungs are filled with fluid containing:
 - **Chloride**
 - **Minimal protein**
 - **Mucus**
 - **Surfactant**
- Fetal breathing movements occur in utero to promote lung growth and amniotic fluid aspiration.

High-Yield Points

- **Lung buds** form from the **endodermal foregut** around **week 4** .
- **TEF + EA** are common congenital malformations; always consider **VACTERL** association.
- **Surfactant production begins** ~ **week 24** , but surfactant surge occurs at ~**week 34–36** .
- **Mature alveoli** continue developing **into early childhood** (~8 years).
- Lung branching is driven by **FGF10 signaling** from mesenchyme.
- **Tracheoesophageal septum** divides respiratory and digestive tracts.