The Respiratory System

Wednesday, August 20, 2025 3:35 PM

📖 Embryology – Respiratory System

🟤 Formation of the Lung Buds

- At ~4 weeks of development, the respiratory diverticulum (lung bud) appears as a ventral outgrowth from the foregut.

- Its *appearance and position* are dependent on:

    - ⬆ Retinoic acid (RA) produced by adjacent mesoderm →
    - Upregulation of TBX4 transcription factor in the endoderm of the gut tube.
    - TBX4 → induces formation, growth, and differentiation of the developing lung.

    #### 🔍 Important MCQ Point

    TBX4 is the key transcription factor responsible for initiating lung development.

- Germ layer origins:

    - Endoderm → epithelium of larynx, trachea, bronchi, and lungs.

- Splanchnic mesoderm → cartilage, muscle, and connective tissue of trachea and lungs.

Separation of Lung Bud from the Foregut

- Initially lung bud is in open communication with the foregut.
- As the diverticulum grows caudally, two longitudinal ridges form → tracheoesophageal ridges.
- Fusion of these ridges forms the tracheoesophageal septum, which divides the foregut into:
  - Dorsal part → esophagus
  - Ventral part → trachea + lung buds
- Communication with pharynx remains through the laryngeal orifice.

Clinical Correlates

Tracheoesophageal Fistulas (TEFs) & Esophageal Atresia

- Cause: Abnormal partitioning of esophagus and trachea by tracheoesophageal septum.
- Incidence: ~1/3,000 births.

- Most common type (~90%):
    - Upper esophagus ends blindly
    - Lower segment forms a fistula with trachea
- Other types:
    - Isolated esophageal atresia → 4%
    - H-type TEF without esophageal atresia → 4%
    - Remaining rare variations → ~1% each

Associated Conditions

- Frequently associated with other congenital anomalies (33% have cardiac defects).
- Part of VACTERL association:
    - Vertebral anomalies
    - Anal atresia
    - Cardiac defects
    - Tracheoesophageal fistula
    - Esophageal atresia
    - Renal anomalies
    - Limb defects

Complications

- Polyhydramnios:

- Swallowed amniotic fluid cannot reach the stomach/intestines in some TEF types.

- Postnatal risks:

  - Gastric contents / amniotic fluid may enter trachea via fistula → pneumonitis, pneumonia

Development of the Larynx

Germ Layer Origins

- Endoderm → internal *epithelial lining* of the larynx

- Mesenchyme of 4th & 6th pharyngeal arches → cartilages + muscles of larynx

Morphological Changes

- Rapid proliferation of arch mesenchyme causes the laryngeal opening to change:

  - Initially → sagittal slit
  - Later → becomes T-shaped

- Mesenchyme differentiates into thyroid, cricoid, and arytenoid cartilages, resulting in the adult appearance of the laryngeal orifice.

Recanalization Phase

- Laryngeal epithelium proliferates → temporarily occludes lumen
- Vacuolization & recanalization form laryngeal ventricles
    - These are bordered by folds → become false and true vocal cords

Innervation (⚠ Frequently Asked)

- All laryngeal muscles derive from 4th & 6th arches → supplied by Vagus nerve (CN X)
    - Superior laryngeal nerve → derivatives of 4th arch
    - Recurrent laryngeal nerve → derivatives of 6th arch

🟤 Trachea, Bronchi, and Early Lung Development

- As the lung bud separates from the foregut → forms trachea + two bronchial buds
- Week 5:
    - Each bronchial bud enlarges → right & left main

bronchi
    - Right → forms 3 secondary bronchi (→ 3 lobes)
    - Left → forms 2 secondary bronchi (→ 2 lobes)

Expansion of Lung Buds

- Grow caudally & laterally into pericardioperitoneal canals

- These canals gradually narrow and become separated by:

    - Pleuroperitoneal folds (→ separates from peritoneal cavity)
    - Pleuropericardial folds (→ separates from pericardial cavity)

- Remaining space → primitive pleural cavities

Pleura Formation

Structure	Germ Layer Origin	Fate
Mesoderm covering lung surface	Splanchnic mesoderm	Visceral pleura
Mesoderm lining	Somatic	Parietal pleura

the body wall	mesoderm	
Space between them	—	Pleural cavity

Branching of Bronchial Tree

- Secondary bronchi → divide dichotomously
- Form:
  - 10 segmental (tertiary) bronchi in right lung
  - 8 segmental bronchi in left lung
  - → basis of bronchopulmonary segments
- By 6th month → ≈17 generations of branches formed
- After birth → ~6 more generations occur

  Regulation of branching = epithelial–mesenchymal interactions

  Signals originate in splanchnic mesoderm (e.g. FGF family)
- As branching continues, lungs gradually shift caudally → at birth, tracheal bifurcation is at T4

level

📊 Maturation of the Lungs

Stage	Weeks	Key Features
Pseudoglandular	5–16 wk	Formation of terminal bronchioles only; no respiratory bronchioles or alveoli
Canalicular	16–26 wk	Respiratory bronchioles form → divide into alveolar ducts
Terminal sac period	26 wk – birth	Terminal sacs (primitive alveoli) develop; capillaries contact epithelium

Alveolar period	8 months – childhood	Formation of mature alveoli with well-developed epithelium–capillary contacts

Maturation of the Lungs

Canalicular Phase (up to 7th month)

- Bronchioles continuously divide into smaller respiratory bronchioles
- Vascular supply increases steadily
- Each respiratory bronchiole → 3–6 alveolar ducts
- Ducts terminate in terminal sacs (primitive alveoli) → lined by flat alveolar cells closely associated with capillaries
- End of 7th month → enough terminal sacs & capillaries present → premature infant can survive

Late Fetal / Terminal Sac Period (last 2 months +

postnatal years)

- Number of terminal sacs increases steadily
- Type I alveolar epithelial cells become thinner → capillaries protrude into sacs
- Formation of blood–air barrier (thin epithelium + capillary endothelium)
- Type II alveolar epithelial cells appear (~end of 6th month)
    - Function → produce surfactant
    - Surfactant = phospholipid-rich fluid → ↓ surface tension at air–alveolar interface

Before Birth

- Lungs are filled with fluid containing:
    - High chloride, little protein
    - Mucus from bronchial glands
    - Surfactant (from type II cells)
- ↑ surfactant production near 34th week
    - Small amount enters amniotic fluid → activates

macrophages
    - Macrophages migrate → produce IL-1β
    - → ↑ prostaglandin production → initiates uterine contractions
        - *Fetal surfactant may help trigger labor*

Fetal Breathing Movements

- Begin before birth
- Cause aspiration of amniotic fluid
- Help stimulate lung development and train respiratory muscles

At Birth

- Fluid in alveoli is rapidly absorbed (blood/lymph vessels)
- Surfactant remains on alveolar surface → prevents collapse during expiration
- First breath → lungs expand and fill pleural cavities

Clinical Correlate – Surfactant and RDS

Condition	Mechanism / Feature

Respiratory Distress Syndrome (RDS)	Insufficient surfactant → ↑ surface tension → alveoli collapse (atelectasis) during expiration
Frequency	~20% of deaths in premature newborns
Histology	Alveoli partially collapsed, contain protein-rich fluid, hyaline membranes, lamellar bodies
Management	Artificial surfactant therapy + Maternal glucocorticoids (stimulate fetal surfactant production)

Congenital Lung Abnormalities

Abnormality	Description / Significance
Blind-ending trachea / absence of lungs / lung agenesis	Very rare
Abnormal bronchial	More common; may → supernumerary lobules (usually

branching	clinically insignificant, but may complicate bronchoscopy)
Ectopic lung lobes	Arise from trachea or esophagus → due to extra respiratory buds
Congenital lung cysts	Dilated terminal or larger bronchi → honeycomb appearance on imaging; drain poorly, often → chronic infections

Postnatal Lung Development

- Respiratory movements at birth → air enters lungs → expands alveoli
- Lung growth after birth:
    - Mainly due to increase in number of respiratory bronchioles and alveoli
    - Only ~1/6 of adult alveoli are present at birth
    - Remaining alveoli form over the first ~10 years of life