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Development of the respiratory system

Learning objectives:

- ✓ **Describe the development of the different parts of the respiratory system.**
- ✓ **Identify the possible congenital anomalies.**

Formation of the lung buds:

- When the embryo is approximately 4 weeks old, the respiratory diverticulum (lung bud) appears as an outgrowth from the ventral wall of the foregut. Hence epithelium of the internal lining of the larynx, trachea, bronchi and the lungs, is of endodermal origin.
- The cartilaginous, muscular and connective tissue components of the trachea and lungs are derived from splanchnic mesoderm surrounding the foregut.
- Initially the lung bud is in open communication with the foregut. When the diverticulum expands caudally, two longitudinal ridges (the tracheoesophageal ridges) separate it from the foregut. When these ridges fuse to form the tracheoesophageal septum, the foregut is divided into a dorsal portion (the esophagus) and a ventral portion (the trachea and lung buds).
- The respiratory primordium maintains its communication with the pharynx through the laryngeal orifice.

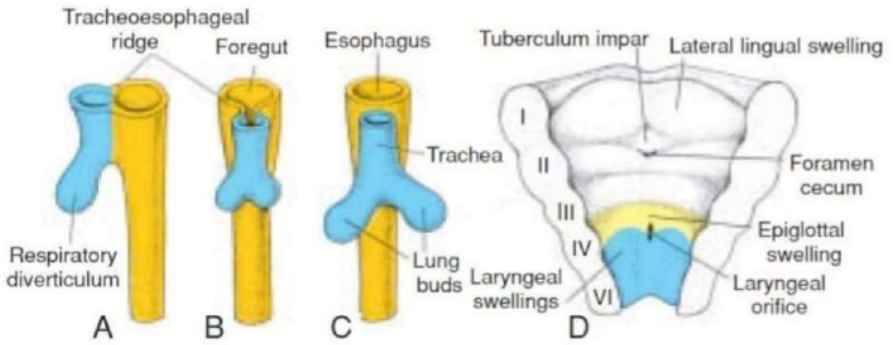

Figure 1 (A, B, and C): Successive stages in development of the respiratory diverticulum showing the tracheoesophageal ridges and formation of the septum, splitting the foregut into esophagus and trachea with lung buds. **(D)** The ventral portion of the pharynx seen from above showing the laryngeal orifice and surrounding swelling.

Larynx:

- The internal lining of the larynx originates from endoderm.
- The cartilages and muscles originate from mesenchyme of the fourth and sixth pharyngeal arches.
- At about the time that the cartilages are formed, the laryngeal epithelium proliferates rapidly, resulting in a temporary occlusion of the lumen. Subsequently, vacuolization and recanalization produce a pair of lateral recesses, the laryngeal ventricles. These recesses are bounded by folds of tissue that differentiate into the false and true vocal cords.
- Since musculature of the larynx is derived from mesenchyme of the fourth and sixth pharyngeal arches, all laryngeal muscles are innervated by branches of the vagus nerve:
    1. The superior laryngeal nerve innervates derivatives of the fourth pharyngeal arch.
    2. The recurrent laryngeal nerve innervates derivatives of the sixth pharyngeal arch.

Trachea, Bronchi and Lungs:

- During its separation from the foregut, the lung bud forms the trachea and two lateral outpocketings called the bronchial buds.
- At the beginning of the fifth week, each of these buds enlarges to form right and left main bronchi. The right then forms three secondary bronchi, and the left forms two.
- During further development, secondary bronchi divide repeatedly forming 10 segmental bronchi in the right lung and 8 in the left, creating the bronchopulmonary segments of the adult lung.
- 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 the fourth thoracic vertebra.

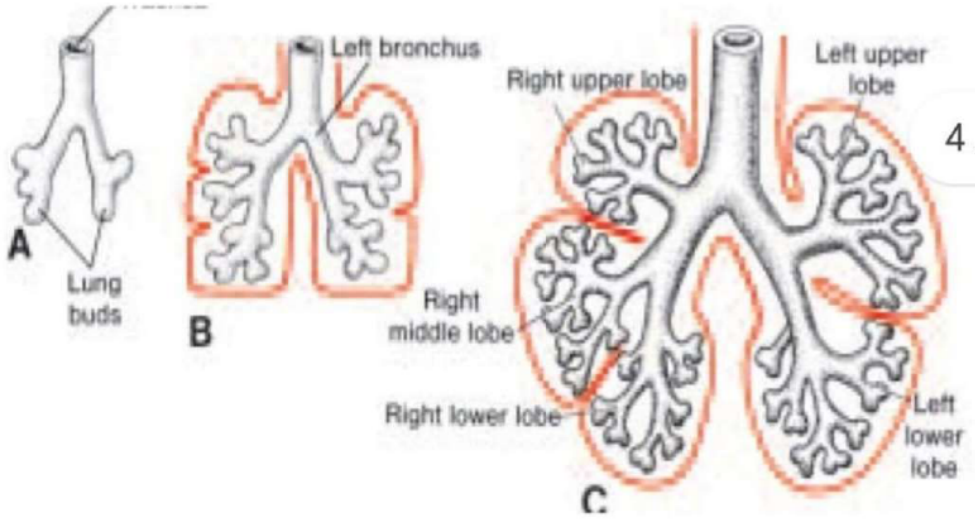

Figure 2: Stages in development of the trachea and lungs. A. 5 weeks. B. 6 weeks. C. 8 weeks

Maturation of the Lungs:

- Up to the seventh prenatal month, the bronchioles divide continuously into more and smaller canals.
- Respiration becomes possible when some of the cells of the cuboidal respiratory bronchioles change into thin flat cells. These cells are intimately associated with numerous blood capillaries, and the surrounding spaces are now known as terminal sacs or primitive alveoli.
- During the last 2 months of prenatal life, the number of terminal sacs increases steadily. In addition, cells lining the sacs, known as type I alveolar epithelial cells, become thinner.
- At the end of the sixth month, type II alveolar epithelial cells develop and produce surfactant, a phospholipid-rich fluid capable of lowering surface tension at the air-alveolar interface.
- It is estimated that only one-sixth of the adult number of alveoli are present at birth.

Clinical notes:

- ✓ Abnormalities in partitioning of the esophagus and trachea by the tracheoesaphageal septum result in esophageal atresia with or without tracheoesaphageal fistulas.

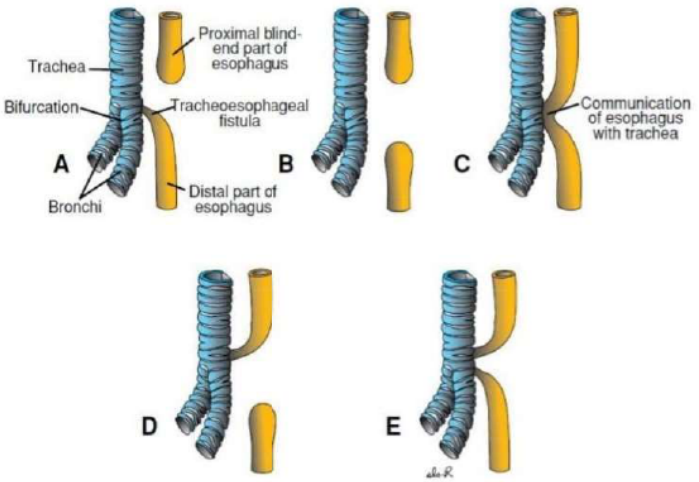

Figure 3: Various types of esophageal atresia and/or tracheoesophageal fistulae. A. The most frequent abnormality (90% of cases) occurs with the upper esophagus ending in a blind pouch and the lower segment forming a fistula with the trachea. B. Isolated esophageal atresia (4% of cases). C. H-type tracheoesophageal fistula (4% of cases). D and E. Other variations (each 1% of cases).

- ✓ Many abnormalities of the lung and bronchial tree have been described such as agenesis of one lung, congenital cysts.
- ✓ Surfactant is important for survival of the premature infant. When surfactant is insufficient, respiratory distress syndrome develops. This is a common cause of death in the premature infant.

References:

1. Saddler, T.W. (2020): Langman`s medical embryology, chapter 12: 275-284.
2. Kaplan (2021): Lecture Notes (anatomy), chapter 2.