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1. Development of the lungs

Successful development and function of the lung requires the completion of both physical development, required for the structure of the lung, and biochemical development of the surfactant system, required for the stability of this very large surface area. The two processes clearly are related.

Incomplete development of lung structure and premature birth prior to the development of the surfactant system will lead to respiratory compromise or insufficiency in the newborn. The stages of lung development are summarized in the table.

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| Pseudoglandular period | 5- 16 weeks | Branching has continued to form terminal bronchioles. No respiratory bronchioles or alveoli are present |
| Canalicular period | 16- 26 weeks  | Each terminal bronchioles divides into 2 or more respiratory bronchioles, which in turn divides into 3-6 alveolar ducts  |
| Terminal sac period  | 26 weeks to birth | Terminal sacs(primitive alveoli) form, and capillaries establish close contact  |
| Alveolar period | 8 months to childhood  | Mature alveoli have well developed epithelial endothelial(capillary) contacts |

There are five phases of structural lung development that occur at progressive times during gestation. The timing of the phases is approximate, with variation between fetuses, and in fact, there is no absolute agreement about the weeks that comprise each phase among various authors and texts. The embryonic stage is apparent in the 3 week old embryo. The lung bud develops from the foregut and in communication with it. Separation of the two lung buds comes about with fusion of the esophagotracheal ridges to form the esophagotracheal septum. When the embryo is 5 weeks old, two primary lung buds are identifiable. The lung buds go on to form their first subdivisions, with 3 lobar buds developing in the right lung bud and 2 lobar buds developing in the left. These are the forerunners of the right upper, middle and lower lobes and the left upper and lower lobes. Development progresses in the 8 week old embryo as the lobar buds subdivide and form the bronchopulmonary segments. Lung buds are lined by endodermally derived epithelium which differentiates into respiratory epithelium that lines the airways and specialized epithelium that lines the alveoli. The innervation of the lungs is derived from ectoderm, while the mesoderm is the origin of pulmonary blood vessels, smooth muscle, cartilage and other connective tissue.The pseudoglandular stage takes place between the 7th and 16th week of embryonic development. Conducting airways are formed by progressive branching. This is a demonstration of the power of 2n. Eventually 16-25 generations of primitive airways are formed. Endodermal lung buds undergo branching only if they are exposed to bronchial mesoderm.

The rate and extent of branching appear directly proportional to amount of mesenchyme present. Allbronchial airways are formed by 16 weeks. After this time, further growth occurs by elongation and widening of existing airways.During this stage, the first differentiation of lung epithelium occurs. By 13 weeks cilia appear in the proximal airways. Mesenchyme is necessary for this epithelial differentiation to occur and there is a transition from formation of bronchial epithelial cells (ciliated columnar and goblet cells) to alveolar type II cells. Conversely, the differentiation of lung mesenchyme requires the presence of lung epithelium.

The canalicular stage takes place between the 16th and 25th week. At this time the gas exchanging portion of the lung is formed and vascularized. There is a decrease of interstitial tissue and growth of the capillary network. By 20 weeks there is differentiation of the type I pneumocyte. The type I pneumocyte is the primary structural cell of the alveolus, and gas exchange will occur across these very thin, membrane-like cells. Capillaries begin to grow in absolutely close proximity to the distal surface of the alveolar cells (if the potential alveolar space is considered proximal. At about the same time, there is the appearance of lamellar bodies, also called inclusion bodies, in type II alveolar cells. The lamellar body is the site of surfactant storage, prior to its release into the alveolar space. The terminal sac, or saccular stage encompasses the period from 26 weeks until term. During this stage, there is a decrease in interstitial tissue, and a thinning of the airspace (alveolar) walls. As this stage progresses, there are recognizable Type I and Type II cells. The lamellar bodies of the Type II cells are the site of storage of surfactant, which is rich in phosphatidylinositol (vs. phospahatidyl choline and phosphatidyl glycerol in late gestation lungs), and is necessary for alveolar stability. The stability of the lung at birth correlates with the number of lamellar bodies present. In the absence of surfactant, the lung can maintain alveoli in an open state for only a very short time. At birth, the air-containing space, later to become the alveolus, has been called a “primitive saccule”. There are approximately 20x106 saccules at birth. The saccules continue to mature following birth in the postnatal or alveolar stage. While these saccules are lined by mature Type I cells, the shape or geometry of the saccules does not achieve “adult” configuration until approximately 5 weeks after birth. The functioning alveolus is connected to an alveolar duct, is lined with Type I cells, which are in intimate contact to pulmonary capillaries, contain surfactant produced by Type II cells and

have pores (pores of Kohn) connecting them to adjacent alveoli. The interstitial capillaries are exposed to two alveoli simultaneously. The air/blood interface consists of the Type I cell, a very thin basement membrane and the pulmonary capillary endothelium. At functional maturity, there are approximately 300x106 alveoli in the lung. This number of alveoli appears to be achieved by the age of 8. The development of the pulmonary arterial system follows a similar progression to that of the developing airways. Development of, and branching of the pulmonary artery mirrors bronchial branching, and later mirrors alveolar development. By the beginning of the cannalicular stage arteries in the preacinar region have formed. The development of muscle within the wall of the pulmonary blood vessels lags behind structural development. Muscularization of intra-acinar arteries does not keep pace with the appearance of new arteries and is not complete until childhood. What is the significance of this? Although the control of pulmonary blood flow in terms of distribution within the lung is controlled by a number of factors (physical location of lung units, gravity, oxygen, nitric oxide), alveolar oxygen tension is probably the most important determinant of pulmonary blood flow.

The ultimate effector governing the distribution of pulmonary blood flow is pulmonary vascular muscle. The process of hypoxic pulmonary vasoconstriction governs this distribution of blood flow. Decreased alveolar oxygen tension will cause vasoconstriction in the area of the alveolus with a decreased oxygen tension, thus diverting blood to better oxygenated areas of the lung. During a generalized decrease in oxygen tension, or hypoxia, there is vasoconstriction of pulmonary blood vessels throughout the lung which causes a rise in pulmonary artery pressure. Why is there so little blood flow in the pulmonary artery in the fetus, and why does this suddenly change with the first breath after birth? The fetal alveolus is filled with liquid not exposed to the atmosphere, and therefore oxygen tension in the alveolus is very low. As a consequence of this low oxygen tension in the alveolus, there is generalized pulmonary vasoconstriction, a rise in pulmonary artery pressure, and diversion of blood from the pulmonary bed, across the ductus arterious to the systemic circulation. At birth, as the alveoli become gas filled, and oxygen tension in the alveolus rises, vasoconstriction decreases, and blood flow now increases to the lung.

2) Rotation of the stomach and the formation of omental bursa

The primordium of the primitive stomach is visible about the end of the fourth week.  It is initially oriented in the median plane and suspended from the dorsal wall of the abdominal cavity by the dorsal mesentery or mesogastrium.  During development the stomach rotates 90� in a clockwise direction along its longitudinal axis, placing the left vagus nerve along its anterior side and the rightvagus nerve along its posterior side.  Rotation of the stomach creates the omentalbursa or lesser peritoneal sac.

The **omental bursa** or **lesser sac** is a hollow space that is formed by the [greater and lesser omentum](https://www.kenhub.com/en/library/anatomy/greater-and-lesser-omentum) and its adjacent organs. It communicates with the greater sac via the epiploic foramen of winslow, which is known as the general cavity of the [abdomen](https://www.kenhub.com/en/library/anatomy/abdomen-and-pelvis) that sits within the [peritoneum](https://www.kenhub.com/en/library/anatomy/the-peritoneum), but outside the lesser sac. This space has well-defined borders which are represented by certain organs or their parts, so they are quite easy to spot and form a mental image of the omental bursa. In addition, like anything in anatomy, the omental bursa doesn't just exist as a standalone and isolated entity, but rather it communicates with several other spaces and recesses found throughout the body.

The borders of the omental bursa are demarcated as follows:

* **anteriorly** by the [quadrate lobe of the liver](https://www.kenhub.com/en/library/anatomy/functional-division-of-the-liver), the gastrocolic ligament and the lesser omentum
* to the **left** it is limited by the left [kidney](https://www.kenhub.com/en/library/anatomy/kidneys) and the left [adrenal gland](https://www.kenhub.com/en/library/anatomy/adrenal-glands)
* **posteriorly** it is walled off by the [pancreas](https://www.kenhub.com/en/library/anatomy/the-pancreas)
* to the **right**, the epiploic foramen and lesser omentum can be found and the greater sac beyond that.

3) Development of the oesophgus

Gut and more specifically esophageal development are most easily understood starting at week four. At this stage, the early embryo consists of three distinct layers, in what is known as a trilaminar disc, connected to the yolk sac. The trilaminar disc is composed of outer ectoderm, middle mesoderm, and an inner layer known as the endoderm. The layers orient in such a way that the endoderm layer is in contact with the outer ectoderm layer at the poles of the embryo. At the start of the fourth week, folding occurs such that corresponding cranial, caudal, and lateral edges of the disc come together. This folding occurs through the ventral midline, and the layers fuse allowing for internalization of the endoderm layer, such that the embryo takes on a tube within a tube configuration, an inner tube composed of endoderm and an outer tube consisting of ectoderm, and between the two layers, mesoderm.

Initially, this inner tube is blind-ended at both poles and is the precursor to the final digestive tract. The inner tube itself divides into three anatomical parts, the foregut, midgut, and hindgut. The foregut being the most cranial portion and hindgut the most caudal. The foregut and hindgut delineation is the center component, the midgut, which is continuous with the yolk sac through the vitelline duct. The mechanisms of early folding and tube position have their basis in concentration-dependent signaling which sets up a ventral-dorsal, rostral-caudal, and left-right axis. These axes are influenced by and contribute, in a reciprocal manner to local endodermal and mesodermal interactions. The component of the foregut that will give rise to the esophagus also will give rise to the trachea and lungs. From the foregut endoderm will arise the esophageal epithelium as well as mucosal glands. The mesodermal layer surrounding the foregut will give rise to the striated muscular and smooth muscle layers of the esophagus.  These processes are associated with numerous signaling molecules. However, the first step of esophageal organogenesis from the foregut is the differentiation of the foregut cells into the trachea, lung, and esophagus. This process begins with the cellular expression of many genes.

After esophageal specification occurs, several notable changes are visible in the developing embryo. At approximately week 6 of development, the circular and longitudinal muscular layers begin to form, and ganglion cells of the myenteric plexus first present. Moving into week 7, cells of mesodermal origin proliferate into the submucosal layer forming the eventual blood supply to the esophagus. The muscular layers which began in week 6, are completed by the 9th week.[[5]](https://www.ncbi.nlm.nih.gov/books/NBK542304/#article-32469.r5) Rostral-caudally, a distinction occurs in the muscular subtypes found within the esophagus. The cranial third of the esophagus contains mostly striated muscle, the caudal third transitions into mostly smooth muscle, and the middle third being a combination of both muscular subtypes. Along with this change in musculature, cranially to caudally, there is hypothesized to be a dual set of innervation of these layers from the enteric nervous system and the vagal nerve, which is a product of branchial arch 6.