**My assignment 1**

**Name: Adesina Benita tomisin**

**Department: human anatomy**

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## Questions

Write notes on the following:

I) Development of the lungs

II) Rotation of the stomach and the formation of the Omental bursa

III) Development of the esophagus

**ANSWERS**

**1. DEVELOPMENT OF THE LUNGS**

Lung development is subdivided into three main periods  the embryonic period, the fetal period and postnatal lung development. Lung organogenesis is part of the embryonal period. While fetal lung development consists in the pseudoglandular, canalicular and saccular stages, postnatal lung development comprises the stages of classical and continued alveolarization, as well as of microvascular maturation. The phases of lung development are mainly based on morphological criteria. Because most processes during lung development start proximal and extend into the periphery, all phases of lung development overlap

The development of the lungs are in week 4-7

In humans at day 26 , the anlage of the right and left lungs appears as two independent out pouchings of the ventral wall of the primitive foregut The two lung buds are located right and left of the anlage of the trachea . They are not the result of the first branching of a common lung bud as postulated earlier . Both lung buds begin elongating and start a repetitive circle of growth into the surrounding mesenchyme and branching.

The primitive foregut divides into the esophagus and trachea after a deepening and joining of the laryngotracheal sulci of the lateral walls of the foregut. Mesenchymal cells surrounding the forming trachea are condensing focally and differentiate into precursors of cartilage towards the end of the embryonic period. With further development of the bronchial tree, the formation of the cartilage moves distally until it reaches the smallest bronchi (25 weeks).

During weeks 5–7, the visceral pleura forms as a product of the splanchnic mesoderm. In parallel, the parietal pleura forms out of the somatic mesoderm layer covering the inner surface of the body wall. Thereafter, the visceral pleura starts to fold into the lung separating the tissues surrounding the lobar bronchi. It forms the lobar fissure separating the lung lobes. In parallel with the formation of the pleura, the pleuropericadial folds meet and fuse with the foregut mesenchyme. Caudally at the posterior body wall, the two pleuroperitoneal membranes start growing towards the posterior edge of the septum transversum. All of them meet and fuse, resulting in a closure of the pleural cavities.

Because the anlage of the lungs forms out of the primitive foregut, the future lung epithelia are of endodermal descent. The mesoderm, where the epithelial tubes push in, is obviously of mesodermal descent. The dual descent of the lung tissue is of importance for the branching morphogenesis, because branching is governed by an intensive cross-talk between epithelial and mesenchymal cells and the factors they are producing. The epithelial cells are supported by a basement membrane and surrounded by an extracellular matrix that is in large parts produced by the mesenchymal cells. The components of the extracellular matrix including the basement membrane are different at the terminal bud, the branching points and in the more proximal parts of the bronchial tree where epithelial differentiation already started . A very specific differential expression of factors like fibroblast growth factor 10 (FGF-10), bone morphogenic protein 4 (BMP-4), Sonic Hedgehog (Shh), retinoic acid, Notch, TGF-β and others give the instructions for the branching morphogenesis. During this process, the epithelial tubes go through repetitive circles of branching and outgrowth into the surrounding mesenchyme

The pulmonary arteries are running in parallel to the airways, delivering the blood to the capillary network of the alveoli. The pulmonary veins collect the blood and run inter-axially at the surface of the pulmonary units, be it segments, sub-segments or as the smallest unit the acini. The veins are embedded in the inter-axial connective tissue. In order to reach the hilum, the large venous branches join the arteries and airways in the most central areas. The first pulmonary vessels are formed as a plexus in the mesenchyme surrounding the lung buds by vasculogenesis—the formation of vessels due to a differentiation of mesenchymal cells. The plexus is cranially connected to the aortic sac and caudally to the left atrium. During branching of the future airways, a new capillary plexus is formed as a halo surrounding each newly formed bud. Each plexus adds to the future pulmonary circulation. The final structure is achieved by intussusceptive re modeling, pruning and angiogenesis of the primary formed vessels. Thus, the forming bronchial tree of airways serves as a template for the vascular tree of blood vessels and lymphatic drainag.

**Clinical aspects of the embryonic period**

Malformations during organogenesis are often related to lung bud formation and development, tracheal/esophageal separation and an incomplete formation of the diaphragm. As for any other organ, these abnormalities show a high mortality and postnatal morbidity. Structural malformations like pulmonary agenesis or aplasia, as well as pulmonary valve stenosis are generally viewed as nonsurvivable, whereas others show variable degrees of morbidity. An incomplete closure of the pericardial–peritoneal canals causes a diaphragmatic hernia and a compression of the developing lung resulting in pulmonary hypoplasia . A variety of permutations of abnormal connections between the trachea and the esophagus represent a common congenital malformation during pulmonary organogenesis. It includes tracheaoesophageal fistula and esophageal atresia, a defect where the upper and lower segments of the esophagus do not connect. In full-term infants, the postsurgical survival is high but in low-birth-weight babies, these malformations are often accompanied by other congenital defects resulting in a higher risk for poor outcomes.

2. Rotation of the stomach and formation of the omental bursae

Rotation of the stomach

It starts at week 5, in a spindle-shaped tube, there are about 3 stages for the rotation of the stomach.

in the first stage,

Ventral and dorsal mesenteries attach the tube to the body walls

Recall that the portion of the dorsal mesentery that anchors the stomach can be more specifically referred to as the dorsal mesogastrium.

Branches of the left and right vagus nerves lie on ventral and dorsal surfaces.

Recognize that this is a simplification, as fibers from the right and left vagal plexuses intermix with each other and the celiac plexus, to some degree

In the second stage of turning,

Differential growth of the stomach and clockwise rotation along the longitudinal axis alters the course of the vagus nerve branches:

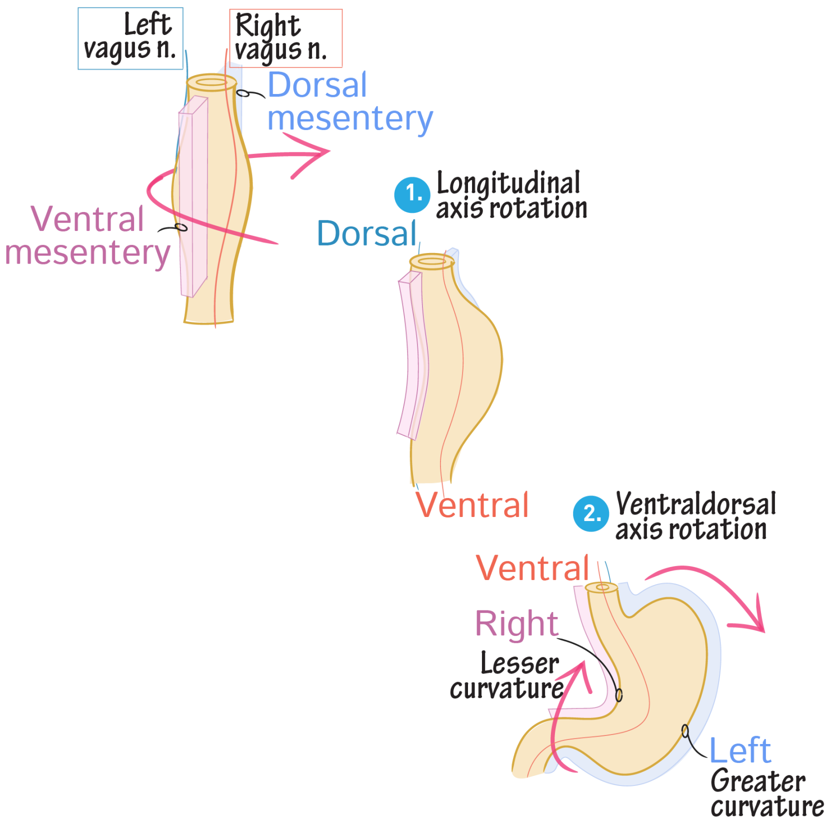
The right vagus nerve now innervates the anterior/ventral surface of the stomach

The left vagus nerve lies on the posterior aspect

In the third stage we'll notice that the cephalic and caudal ends remain in the midline.

As the stomach rotates along the ventral-dorsal (aka, antero-posterior) axis, the caudal end

## Rotation of the Stomach




is displaced towards the right, as the cephalic end towards the left;

The ventral and dorsal mesenteries are also displaced to the right and left, respectively.

Lesser curvature = ventral mesentery attachment.

Greater curvature = dorsal mesentery attachment.

Though not shown here, the ventral mesentery gives rise to the falciform ligament, which secures the liver ventrally, and, the lesser omentum, which connects the liver and stomach and proximal duodenum.

The dorsal mesentery gives rise to the greater omentum, the apron-like fold of mesentery that attaches to the greater curvature of the stomach and drapes over the small intestine.

3. **The development of the oesophagus**

Th development of the oesophagus starts at the 4th week of development

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.[3] 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.[2][4]

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] 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.[6][7] 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.

Co-innervation of muscle cells is hypothesized to allow for early peristalsis after birth while the nervous system is not fully mature. The process of esophageal innervation occurs throughout the development of the embryo and requires proliferation and migration of neural crest cells which migrate rostrally-caudally through the gut tube starting during the 4th week and ending their migration around the 9th week of development.[8] Setting the precursor cells for innervation along the entire gut. During the 6th week, when the muscular layers have begun to form, cells of neuronal crest origin migrate inward between the muscular layers eventually giving rise to the submucosal plexus.[9] This process which began the neuronal development early in the 4th week continues through a slow maturation process which continues after birth.[8] At around the 4th month of development, the columnar epithelium of the foregut begins to undergo a transition into a squamous epithelium a process which will continue well into the third trimester.

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