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Question: Write notes on the following

- **Development of the lungs**

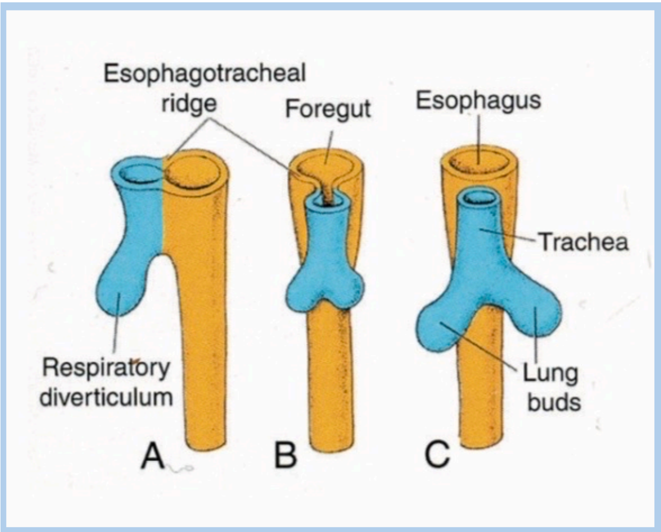
The lungs are derived from the ectoderm, pseudoglandular stage takes place between the 7th and 16th week of embryonic development. Initially, the lung bud is in open communication with the foregut then tracheoesophageal ridges, separate it from the foregut. These ridges fuse to form the tracheoesophageal septum.

The development of the lung is in two phases, lung growth (structural development) and lung maturation (functional development). The lung anlage appears at day 26 as two ventral buds of the foregut at the caudal end of the laryngotracheal sulci.It will give rise to the left and right lung. Both buds elongate, grow into the surrounding mesenchyme, and form the left and right main bronchi (day 32).

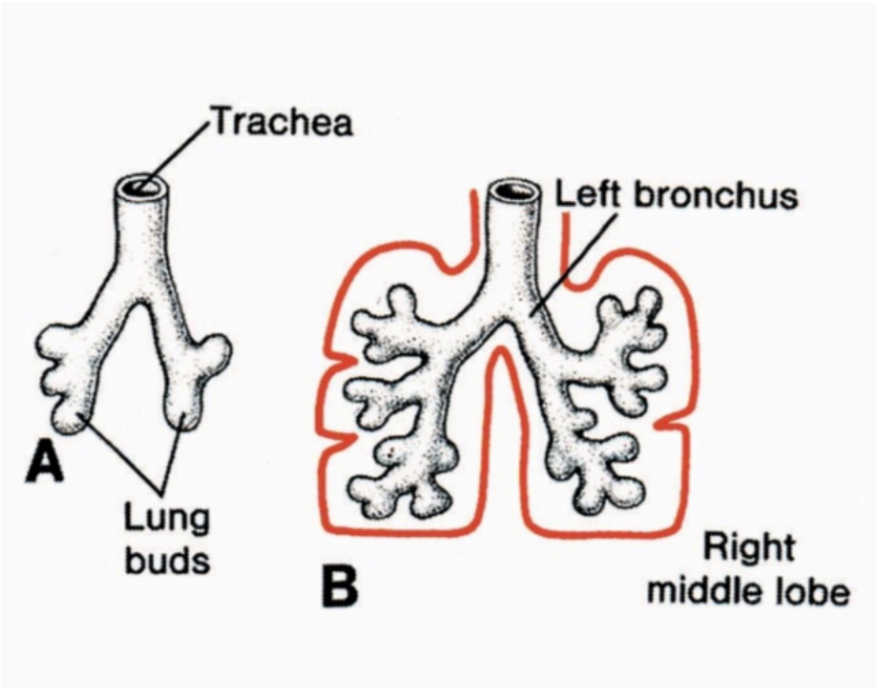
Lung growth can be influenced by a host of physical factors. Lung maturation and the achievement of functionality is primarily biochemical process and is under the control of a number of different hormones. Lung growth proceeds through gestation. There is progressive branching of the airways and finally development of velar spaces capable of gas exchange in the last trimester. The surfactant system, composed of phospholipids that decrease surface tension within the alveoli and prevent alveolar collapse during exhalation, develops in the last trimester, and reaches maturity by approximately 36 weeks. Lung growth continues after birth as alveolar number continues to increase. The end result of the development of the lung is an organ with a tremendously large surface area that is approximately 50-100 m2, capable of exchanging oxygen and carbon dioxide across a very thin membrane.

There are five stages of structural lung development that occur at progressive times during gestation. The timing of the phases is approximate, with variation between foetuses, 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 oesophagotracheal ridges to form the oesophagotracheal septum

When the embryo is 5 weeks old, two primary lung buds are identifiable.



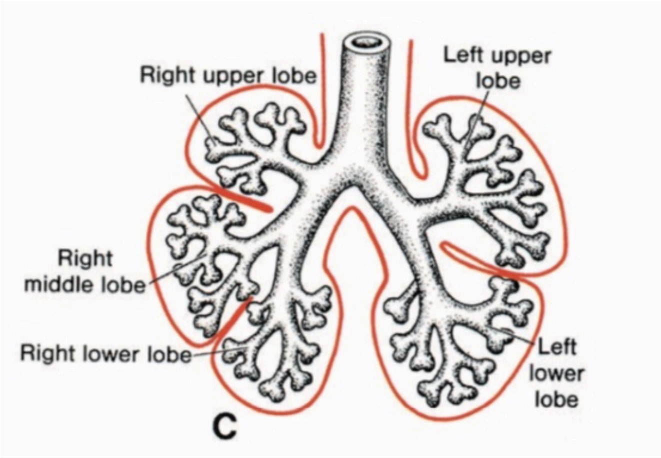
A, B and C, successive stages in development of the respiratory diverticulum showing the esophagotracheal ridges and formation of the septum, splitting the foregut into esophagus and trachea with lung buds.



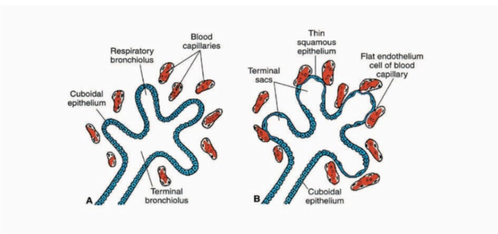
Lungs buds are lined by endodermally derived epithelium which differentiates into respiratory epithelium that lines the airways and specialized epithelium that lines the aveoli. the innervation of the lungs is derived from ectoderm, while the mesoderm is the origin of pulmonary blood vessels , smooth muscle, cartilage and other connective tissue.

the pseudoglandar 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 2. Eventually 16-25 generation of primitive airways are formed. The rate and extent of branching appear directly proportional to amount of mesenchyme present. All branchial airways are formed by 16 weeks. After this time, further growth occurs by enlongation and widening of existing airways.

during this stage, the first differentiation of lung epithelium occurs. by the 13 weeks cilis 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 betwen 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 distall 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 . 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.

Incomplete separation of esophagus and trachea by tracheosophageal septum results in atresia of esophagus with or without tracheosophageal fistula. Defect likely in mesoderm and usually associated with other defects involving mesoderm (cardiovascular malformations, VATER / VACTERL, etc

The growing lung buds expand in caudolateral direction into the pericardioperitoneal canals.
During week 5, the pleuropericardial folds meet and fuse with the foregut mesenchyme.
During weeks 5–7, pleuroperitoneal membranes meet and fuse with the posterior edge of the septum transversum and close the pleural cavities. The visceral pleura have formed by the splanchnic mesoderm, which covers the outside of the lung. Pleura
The parietal pleura have formed by the somatic mesoderm layer covering the inner surface of the body wall. Visceral pleura invaginations of the pleura start to separate the lobar bronchi and give rise to the lobar fissure and the lung lobes.
Branching continues to be regulated by epithelial- mesenchymal interactions.
Organogenesis
Respiratory tract is derived from foregut endoderm and associated mesoderm from endoderm: epithelial lining of trachea, larynx, bronchi, alveoli From splanchnic mesoderm: cartilage, muscle, and connective tissue of tract and visceral pleura.
Growth Factors- Transcription factors likeTTF-1, Gli2, and Gli3; as well as growth factors like FGF-10, TGF-β, BMP-4, SHH, EGF, and VEGF.
Vasculogenesis of the Pulmonary Circulatio**n**
The mesenchyme surrounding the lung buds contains a number of progenitor cells of endothelial cells. The newly formed endothelial cells are connecting to each other to form first capillary tubes. These capillaries coalesce to form small blood vessels alongside the airways, so the earliest pulmonary vessels form by vasculogenesis.
Distal angiogenesis to form branches of vessels.

During fetal life, blood flow through the lung is limited to between 10 and 15 percent of the cardiac output. At birth ductus arteriosus closes and the shunting of the entire cardiac output through the lung.The ductus arteriosus, first obstructed by muscular contraction, and is anatomically closed within a few weeks by the fibrotic organization of an intravascular clot and is known as ligamentum arteriosus.

- Pulmonary hemorrhage
- Necrotizing enter colitis (NEC) and/or gastrointestinal (GI) perforation
- Apnea of prematurity

- **Rotation of the stomach and the formation of the Omental bursa**

The stomach rotates 90 degrees, the spleen is displaced to the left and the liver moves to the right. The peritoneum twists with these movements which lead to the formation of the falciform ligament, the lesser omentum and the coronary ligaments of the liver .The omental bursa or lesser sac is a hollow space that is formed by the 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 that sits within 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.

Borders of the Stomach:

Anteriorly - quadrate lobe of liver, gastro colic ligament, lesser omentum

Left - left kidney, left adrenal gland

Posteriorly - pancreas

Right - epiploic foramen, lesser omentum, greater sac

Communications: Superior recess, splenic recess, inferior recess, folds and recesses around the cecum and duodenum

Borders of the omental bursa.

- Anteriorly by the quadrate lobe of the liver, the gastro colic ligament and the lesser omentum
- To the left it is limited by the left kidney and the left adrenal gland
- Posteriorly it is walled off by the pancreas
- To the right, the epiploic foramen and lesser omentum can be found and the greater sac beyond that.

The cavity itself is almost completely closed, save its communication with the greater sac and the entrance through the omental foramen and is filled with a capillary film. The greater part of the omental bursa consists of its superior recess which extends cranially between the esophagus and the inferior vena cava.

The splenic recess extends to the left between the splenic ligaments and the stomach. Finally, the inferior recess of the omental bursa extends caudally between the stomach and the transverse colon. Other anatomical landmarks of note include a varied number of small peritoneal folds, recesses and fossae which seem to accumulate mostly around the cecum and the duodenum.

Embryology

During embryonic development, the peritoneum is anchored to the gut in the midline of the abdomen anteriorly, with the dorsal mesentery securing it posteriorly. The mesenteric layers develop in an anterior direction around the upper alimentary canal, carrying the blood supply and creating the ventral mesentery.

Due to the growth of the organs, they gradually become larger and have to shift in order to fit into the abdominal cavity. The stomach rotates 90 degrees, the spleen is displaced to the left and the liver moves to the right. The peritoneum twists with these movements which lead to the formation of the falciform ligament, the lesser omentum and the coronary ligaments of the liver. Throughout this entire process, the cavity of the lesser sac is created.

Stomach

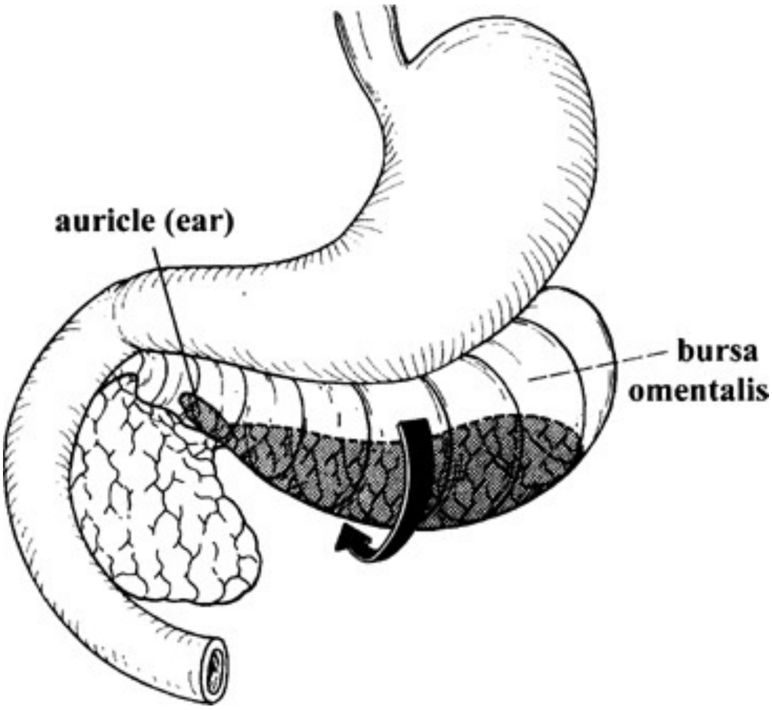
During the fourth week of gestation, the rudimentary stomach appears as a fusiform-shaped dilation of the distal foregut. Subsequently, its appearance and position drastically changes; the latter can be better understood by visualizing a longitudinal axis and an antero-posterior axis around which the stomach rotates.

Posterior part of stomach (ventral view)

The stomach rotates 90 degrees clockwise around its longitudinal axis, resulting in its left side facing anteriorly and its right side posteriorly. This explains why the left vagus nerve innervates the anterior wall, as it once innervated the left side of the stomach, whereas the right vagus nerve innervates the posterior wall, as it once innervated the right side. Concurrent with this rotation, cellular proliferation occurs much faster in the posterior wall of the stomach than in the anterior wall, resulting in the formation of the greater and lesser curvatures, respectively.

Greater curvature of the stomach (ventral view)

The stomach also rotates around its antero-posterior axis, resulting in the caudal end (pyloric part) to move upward and to the right and the cranial end (cardiac part) slightly downward and to the left. Thus, the stomach assumes its final position, with its pylorus located superiorly to the left and its cardia inferiorly to the right.



Pyloric part of the stomach (ventral view)

The rotational changes of the stomach also alter the position of the mesenteries. Recall that the stomach is attached to the dorsal and ventral walls via the dorsal mesogastrium and the ventral mesentery (a.k.a. mesogastrium), respectively. The rotation of the stomach around the longitudinal axis pulls the dorsal mesogastrium to the left and the ventral mesogastrium to the right: this creates a space behind the stomach known as the omental bursa (lesser peritoneal sac).

- **Development of the oesophagus.**

During the third week of gestation, a respiratory diverticulum (lung bud) forms as an outgrowth from the ventral wall of the proximal foregut. While the lung bud continues to expand, it becomes separated from the foregut, which forms the esophagus. Initially, the esophagus is short, but becomes rapidly elongated as a result of the growth and relocation of the heart and lungs.

Esophagus (lateral-left view)

In early embryogenesis, the esophagus develops from the endodermal primitive gut tube. The ventral part of the embryo abuts the yolk sac. During the second week of embryological development, as the embryo grows, it begins to surround parts of the sac. The enveloped portions form the basis for the adult gastrointestinal tract. The sac is surrounded by a network of vitelline arteries. Over time, these arteries consolidate into the three main arteries that supply the developing gastrointestinal tract: the celiac artery, superior mesenteric artery, and inferior mesenteric artery. The areas supplied by these arteries are used to define the midgut, hindgut and foregut.

The surrounded sac becomes the primitive gut. Sections of this gut begin to differentiate into the organs of the gastrointestinal tract, such as the esophagus, stomach, and intestines. The esophagus develops as part of the foregut tube. The innervation of the esophagus develops from the pharyngeal arches.

Function

Swallowing

Food is ingested through the mouth and when swallowed passes first into the pharynx and then into the esophagus. The esophagus is thus one of the first components of the digestive system and the gastrointestinal tract. After food passes through the esophagus, it enters the stomach. When food is being swallowed, the epiglottis moves backward to cover the larynx, preventing food from entering the trachea. At the same time, the upper esophageal sphincter relaxes, allowing a bolus of food to enter. Peristaltic contractions of the esophageal muscle push the food down the esophagus. These rhythmic contractions occur both as a reflex response to food that is in the mouth, and also as a response to the sensation of food within the esophagus itself. Along with peristalsis, the lower esophageal sphincter relaxes.

Reducing gastric reflux

The stomach produces gastric acid, a strongly acidic mixture consisting of hydrochloric acid (HCl) and potassium and sodium salts to enable food digestion. Constriction of the upper and lower esophageal sphincters help to prevent reflux (backflow) of gastric contents and acid into the esophagus, protecting the esophageal mucosa. In addition, the acute angle of His and the lower crura of the diaphragm helps this sphincteric action.

Gene and protein expression

About 20,000 protein-coding genes are expressed in human cells and nearly 70% of these genes are expressed in the normal esophagus. Some 250 of these genes are more specifically expressed in the esophagus with less than 50 genes being highly specific. The corresponding esophagus-specific proteins are mainly involved in squamous differentiation such as keratins KRT13, KRT4 and KRT6C. Other specific proteins that help lubricate the inner surface of esophagus are mucins such as MUC21 and MUC22. Many genes with elevated expression are also shared with skin and other organs that are composed of squamous epithelia.

cancer is still poor, so palliative therapy may also be a focus of treatment.

Main article: Esophageal varices

Esophageal varices are swollen twisted branches of the azygous vein in the lower third of the esophagus. These blood vessels anastomose (join up) with those of the portal vein when portal hypertension develops. These blood vessels are engorged more than normal, and in the worst cases may partially obstruct the esophagus. These blood vessels develop as part of a collateral circulation that occurs to drain blood from the abdomen as a result of portal hypertension, usually as a result of liver diseases such as cirrhosis. : 941–42 this collateral circulation occurs because the lower part of the esophagus drains into the left gastric vein, which is a branch of the portal vein. Because of the extensive venous plexus that exists between this vein and other veins, if portal hypertension occurs, the direction of blood drainage in this vein may reverse, with blood draining from the portal venous system, through the plexus. Veins in the plexus may engorge and lead to varices.

Esophageal varices often do not have symptoms until they rupture. A ruptured varix is considered a medical emergency, because varices can bleed a lot. A bleeding varix may cause a person to vomit blood, or suffer shock. To deal with a ruptured varix, a band may be placed around the bleeding blood vessel, or a small amount of a clotting agent may be injected near the bleed. A surgeon may also try to use a small inflatable balloon to apply pressure to stop the wound. IV fluids and blood products may be given in order to prevent hypovolemia from excess blood loss.