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COURSE TITLE: SYSTEMIC EMBRYOLOGY

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

DEVELOPMENT OF THE LUNGS

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. 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

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. All 12-5 bronchial 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) (Figure 12-5A). 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 (Figure 12-6). 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.

ROTATION OF THE STOMACH AND FORMATION OF THE OMENTAL BURSA

The rotation of the stomach begins at week 5 and starts as a spindle-shaped tube. The ventral and dorsal mesenteries attach the tube to the body walls. The branches of the left and right vagus nerves lie on the dorsal and ventral surfaces. 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
* Notice that the cephalic and caudal ends remain in the midline.

As the stomach rotates along the antero-posterior axis, the caudal end 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.

 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 right vagus nerve along its posterior side.  Rotation of the stomach creates the omental bursa or lesser peritoneal sac.

DEVELOPMENT OF THE ESOPHAGUS

In early [embryogenesis](https://en.wikipedia.org/wiki/Human_embryogenesis), the esophagus develops from the [endodermal](https://en.wikipedia.org/wiki/Endoderm) [primitive gut tube](https://en.wikipedia.org/wiki/Gastrointestinal_tract). The ventral part of the embryo abuts the [yolk sac](https://en.wikipedia.org/wiki/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](https://en.wikipedia.org/wiki/Vitelline_arteries). Over time, these arteries consolidate into the three main arteries that supply the developing gastrointestinal tract: the [celiac artery](https://en.wikipedia.org/wiki/Celiac_artery), [superior mesenteric artery](https://en.wikipedia.org/wiki/Superior_mesenteric_artery), and [inferior mesenteric artery](https://en.wikipedia.org/wiki/Inferior_mesenteric_artery). The areas supplied by these arteries are used to define the [midgut](https://en.wikipedia.org/wiki/Midgut), [hindgut](https://en.wikipedia.org/wiki/Hindgut) and [foregut](https://en.wikipedia.org/wiki/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](https://en.wikipedia.org/wiki/Stomach), and [intestines](https://en.wikipedia.org/wiki/Intestine). The esophagus develops as part of the foregut tube. The innervation of the esophagus develops from the [pharyngeal arches](https://en.wikipedia.org/wiki/Pharyngeal_arch). 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.[[1]](https://www.ncbi.nlm.nih.gov/books/NBK542304/) 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. 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.